

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	8	("6284763" "6458797" "6787553" "6326379" "6576644").pn.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/03/02 14:04
L2	2	"6087368".pn.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/03/02 13:38
L3	49	"PDE5" near5 "IC50"	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/03/02 14:20
L4	30	"PDE5" near5 "IC50" near5 ("100" or "50")	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/03/02 14:19
L5	0	l4 not l3	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/03/02 14:19
L6	0	l2 and "IC50"	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/03/02 14:22
L7	2	"6048864".pn.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/03/02 14:22
L8	0	l7 and "IC50"	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/03/02 14:22
L9	5	("6103738" "6169093" "6365599").pn.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/03/02 14:23
L10	0	l9 and "IC50"	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/03/02 14:23

L11	0	l9 and "IC"	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/03/02 14:27
L12	0	ep-0463756-\$.did.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/03/02 15:28
L13	2	wo-9519978-\$.did.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/03/02 14:31
L14	14844	"IC50"	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/03/02 14:32
L15	162	phosphodiesterase same l14	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/03/02 14:32
L16	159	l15 not l3	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/03/02 14:37
L17	44	l15 and hypertension	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/03/02 15:02
L18	2	wo-9808848-\$.did.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/03/02 15:03
L19	2	wo-9703675-\$.did.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/03/02 15:05
L20	2	wo-9703985-\$.did.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/03/02 15:07

L21	2	wo-9719947-\$.did.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/03/02 15:14
L22	2	wo-9724334-\$.did.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/03/02 15:12
L23	2	"5488055".pn.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/03/02 15:12
L24	2	wo-9518097-\$.did.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/03/02 15:14
L25	2	wo-9807430-\$.did.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/03/02 15:14
L26	54474	(hypertension or (high adj blood adj pressure))	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/03/02 15:15
L27	0	ep-A0463756-\$.did.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/03/02 15:28
L28	0	ep-0463756A-\$.did.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/03/02 15:28
L29	0	ep-A463756-\$.did.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/03/02 15:29
L30	2	ep-463756-\$.did.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/03/02 15:57

L31	355	saralasin	US-PGPUB; USPAT;	OR	OFF	2005/03/02 15:57
L32	319	l31 and angiotensin\$	USOCR; EPO; JPO; DERWENT US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/03/02 15:58
L33	278	l32 and hypertension	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/03/02 17:44
L34	15	(sildenafil adj citrate) same hypertension	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/03/02 17:48
L35	54	candesartan and eprosartan and irbesartan and losartan and olmesartan\$ and telmisartan and valsartan	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/03/02 17:51
L36	4	("4355040" "4880804").pn.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/03/02 17:51
S1	3	("cGMP" or (cyclic adj guanosine adj monophosphate)) near5 (phosphodiesterase\$ or "PDE5") same (angiotensin near3 (receptor adj antagonist))	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/03/01 16:46
S2	14	("cGMP" or (cyclic adj guanosine adj monophosphate)) near5 (phosphodiesterase\$ or "PDE5") and (angiotensin near3 (receptor adj antagonist))	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/03/02 09:58
S3	3	("6458797" "6284763").pn.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/03/01 17:07

S4	19727	sildenafil or viagra or tadalafil or "IC-351" or "IC 351" or cialis or vardenafil or levitra or candesartan or "CV-11974" or "CV 11974" or eprosartan or teveten or "SKF-108566" or "SKF 108566" or irbesartan or "BMS-186295" or "BMS 186295" or "SR-47436" or "SR 47436" or avapro or aprovel or karvea or losartan or cozaar or "dup-753" or "dup 753" or "MK-954" or "MK 954" or (olmesartan adj medoxomil) or "CS-866" or "CS 866" or benicar or olmetec or votum or saralasin or "P-113" or "P 113" or telmisartan or "BIBR 277" or "BIBR277" or "BIBR-277" or pritor or micardis or valsartan or diovan or "CGP-48933" or "CGP 48933" or "CGP48933" or tareg or kalpress or miten or nisis or provas or vals	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/03/01 17:20
S5	1458	sildenafil or viagra or tadalafil or "IC-351" or "IC 351" or cialis or vardenafil or levitra	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/03/01 17:19
S6	18588	candesartan or "CV-11974" or "CV 11974" or eprosartan or teveten or "SKF-108566" or "SKF 108566" or irbesartan or "BMS-186295" or "BMS 186295" or "SR-47436" or "SR 47436" or avapro or aprovel or karvea or losartan or cozaar or "dup-753" or "dup 753" or "MK-954" or "MK 954" or (olmesartan adj medoxomil) or "CS-866" or "CS 866" or benicar or olmetec or votum or saralasin or "P-113" or "P 113" or telmisartan or "BIBR 277" or "BIBR277" or "BIBR-277" or pritor or micardis or valsartan or diovan or "CGP-48933" or "CGP 48933" or "CGP48933" or tareg or kalpress or miten or nisis or provas or vals	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/03/01 17:20
S7	42	(S5 and S6).ti,ab,clm.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/03/01 17:21

S8	319	S5 and S6	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/03/01 17:21
S9	128	S8 and (hypertension or (high adj blood adj pressure))	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/03/01 17:41
S10	2	"6576644".pn.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/03/01 17:41
S11	1458	sildenafil or viagra or tadalafil or "IC-351" or "IC 351" or cialis or vardenafil or levitra	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/03/02 09:58
S12	18588	candesartan or "CV-11974" or "CV 11974" or eprosartan or teveten or "SKF-108566" or "SKF 108566" or irbesartan or "BMS-186295" or "BMS 186295" or "SR-47436" or "SR 47436" or avapro or aprovel or karvea or losartan or cozaar or "dup-753" or "dup 753" or "MK-954" or "MK 954" or (olmesartan adj medoxomil) or "CS-866" or "CS 866" or benicar or olmetec or votum or saralasin or "P-113" or "P 113" or telmisartan or "BIBR 277" or "BIBR277" or "BIBR-277" or pritor or micardis or valsartan or diovan or "CGP-48933" or "CGP 48933" or "CGP48933" or tareg or kalpress or miten or nisis or provas or vals	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/03/02 09:58
S13	319	S11 and S12	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/03/02 09:58
S14	128	S13 and (hypertension or (high adj blood adj pressure))	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/03/02 09:58

S15	128	S14	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/03/02 09:59
S16	115	S15 and ((congestive adj heart adj failure) or angina or stroke or diabet\$)	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/03/02 10:00
S17	0	S16 not S15	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/03/02 10:01
S18	1451	sildenafil or viagra or tadalafil or cialis or vardenafil or levitra	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/03/02 10:02
S19	1767	candesartan or eprosartan or irbesarta or losartan or olmesartan or (olmesartan adj medoxomil) or saralasin or telmisartan or valsartan	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/03/02 10:04
S20	42	(S18 and S19).ti,ab,clm.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/03/02 10:03
S21	42	(S11 and S12).ti,ab,clm.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/03/02 10:04
S22	0	S20 not S21	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/03/02 10:04
S23	1821	candesartan or eprosartan or irbesartan or losartan or olmesartan or (olmesartan adj medoxomil) or saralasin or telmisartan or valsartan	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/03/02 10:04
S24	42	(S18 and S23).ti,ab,clm.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/03/02 10:05

S25	0	S24 not S20	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/03/02 10:05
S26	310	S18 and S23	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/03/02 10:05
S27	187	S26 and (hypertension or hypertensive or (high adj blood adj pressure))	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/03/02 10:05
S28	164	S27 not S24	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/03/02 10:06
S29	53	S28 not S15	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/03/02 10:45
S30	210	S26 and ((congestive adj heart adj failure) or angina or stroke or diabet\$)	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/03/02 10:45
S31	192	S30 not S24	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/03/02 10:46
S32	86	S31 not S15	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/03/02 10:46
S33	139	S31 not S29	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/03/02 10:46
S34	33	S32 not S29	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/03/02 13:27

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alerts (SDIs) affected
NEWS 10 DEC 17 COMPUAB reloaded; updating to resume; current-awareness
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NEWS 11 DEC 17 SOLIDSTATE reloaded; updating to resume; current-awareness
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NEWS 12 DEC 17 CERAB reloaded; updating to resume; current-awareness
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NEWS 13 DEC 17 THREE NEW FIELDS ADDED TO IFIPAT/IFIUDB/IFICDB
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NEWS 17 FEB 25 CA/CAPLUS - Russian Agency for Patents and Trademarks
(ROSPATENT) added to list of core patent offices covered
NEWS 18 FEB 10 STN Patent Forums to be held in March 2005
NEWS 19 FEB 16 STN User Update to be held in conjunction with the 229th ACS
National Meeting on March 13, 2005
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data from INPADOC
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=> file caplus

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SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

0.21

0.21

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FILE COVERS 1907 - 2 Mar 2005 VOL 142 ISS 10

FILE LAST UPDATED: 1 Mar 2005 (20050301/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> e fox david/au

E1	3	FOX DARRELL EUGENE/AU
E2	2	FOX DAVE/AU
E3	44 -->	FOX DAVID/AU
E4	49	FOX DAVID A/AU
E5	9	FOX DAVID B/AU
E6	1	FOX DAVID BRIAN/AU
E7	2	FOX DAVID C/AU
E8	1	FOX DAVID CHARLES/AU
E9	1	FOX DAVID D/AU
E10	1	FOX DAVID E/AU
E11	1	FOX DAVID H/AU
E12	1	FOX DAVID III/AU

=> e

E13	39	FOX DAVID J/AU
E14	1	FOX DAVID JONATHAN/AU
E15	1	FOX DAVID K/AU
E16	6	FOX DAVID L/AU
E17	1	FOX DAVID LEE/AU
E18	1	FOX DAVID LEROY/AU
E19	3	FOX DAVID M/AU
E20	1	FOX DAVID N/AU
E21	12	FOX DAVID N A/AU
E22	10	FOX DAVID NATHAN ABRAHAM/AU
E23	1	FOX DAVID R/AU
E24	1	FOX DAVID S/AU

=> s e2-e3, e20-e22

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      2 "FOX DAVE"/AU
      44 "FOX DAVID"/AU
      1 "FOX DAVID N"/AU
      12 "FOX DAVID N A"/AU
      10 "FOX DAVID NATHAN ABRAHAM"/AU
L1     69 ("FOX DAVE"/AU OR "FOX DAVID"/AU OR "FOX DAVID N"/AU OR "FOX
      DAVID N A"/AU OR "FOX DAVID NATHAN ABRAHAM"/AU)
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=> e hughes bernadette/au

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E1      1 HUGHES BENZIE RHIANNON/AU
E2      2 HUGHES BENZIE RHIANNON M/AU
E3     19 --> HUGHES BERNADETTE/AU
E4      3 HUGHES BERNADETTE M/AU
E5     32 HUGHES BERNARD P/AU
E6      4 HUGHES BERNIE P/AU
E7      3 HUGHES BETH/AU
E8      3 HUGHES BETSY/AU
E9      2 HUGHES BETSY J/AU
E10     1 HUGHES BETSY JANE/AU
E11     1 HUGHES BETSY R/AU
E12     1 HUGHES BILL/AU
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=> s e3-e4

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      19 "HUGHES BERNADETTE"/AU
      3 "HUGHES BERNADETTE M"/AU
L2     22 ("HUGHES BERNADETTE"/AU OR "HUGHES BERNADETTE M"/AU)
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=> e hughes b/au

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E1      6 HUGHES AUSTIN/AU
E2     158 HUGHES AUSTIN L/AU
E3     40 --> HUGHES B/AU
E4      4 HUGHES B A/AU
E5      1 HUGHES B C/AU
E6      5 HUGHES B D/AU
E7      2 HUGHES B F/AU
E8      7 HUGHES B G/AU
E9      2 HUGHES B H/AU
E10     14 HUGHES B J/AU
E11     21 HUGHES B L/AU
E12     13 HUGHES B M/AU
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=> s e3

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L3     40 "HUGHES B"/AU
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=> e fox d/au

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E1      2 FOX CYRIL/AU
E2     27 FOX CYRIL S/AU
E3     75 --> FOX D/AU
E4     25 FOX D A/AU
E5      5 FOX D B/AU
E6     10 FOX D C/AU
E7      3 FOX D E/AU
E8     60 FOX D G/AU
E9      1 FOX D H/AU
E10     18 FOX D J/AU
E11      7 FOX D K/AU
E12     41 FOX D L/AU
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=> e

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E13     3 FOX D M/AU
E14     6 FOX D P/AU
E15     1 FOX D P S/AU
E16     4 FOX D R/AU
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E17	8	FOX D S/AU
E18	20	FOX D W/AU
E19	8	FOX DALE B/AU
E20	1	FOX DALE BENNETT/AU
E21	5	FOX DANIEL/AU
E22	1	FOX DANIEL A/AU
E23	1	FOX DANIEL G/AU
E24	14	FOX DANIEL J/AU

=> e fox d?/au

E1	8	FOX D S/AU
E2	20	FOX D W/AU
E3	0 -->	FOX D?/AU
E4	8	FOX DALE B/AU
E5	1	FOX DALE BENNETT/AU
E6	5	FOX DANIEL/AU
E7	1	FOX DANIEL A/AU
E8	1	FOX DANIEL G/AU
E9	14	FOX DANIEL J/AU,
E10	7	FOX DANIEL JOSEPH/AU
E11	8	FOX DANIEL L/AU
E12	1	FOX DANIEL RICHARD/AU

=> d his

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FILE 'CAPLUS' ENTERED AT 11:49:13 ON 02 MAR 2005

		E FOX DAVID/AU
L1	69 S	E2-E3, E20-E22
		E HUGHES BERNADETTE/AU
L2	22 S	E3-E4
		E HUGHES B/AU
L3	40 S	E3
		E FOX D/AU
		E FOX D?/AU

=> e fox d/au

E1	2	FOX CYRIL/AU
E2	27	FOX CYRIL S/AU
E3	75 -->	FOX D/AU
E4	25	FOX D A/AU
E5	5	FOX D B/AU
E6	10	FOX D C/AU
E7	3	FOX D E/AU
E8	60	FOX D G/AU
E9	1	FOX D H/AU
E10	18	FOX D J/AU
E11	7	FOX D K/AU
E12	41	FOX D L/AU

=> s e3

L4	75	"FOX D"/AU
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=> d his

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FILE 'CAPLUS' ENTERED AT 11:49:13 ON 02 MAR 2005

		E FOX DAVID/AU
L1	69 S	E2-E3, E20-E22
		E HUGHES BERNADETTE/AU
L2	22 S	E3-E4
		E HUGHES B/AU

L3 40 S E3
E FOX D/AU
E FOX D?/AU
E FOX D/AU

L4 75 S E3

=> s 11 or 14

L5 144 L1 OR L4

=> s 12 or 13

L6 62 L2 OR L3

=> s 15 or 16

L7 204 L5 OR L6

=> s 17 and hypertensi?

79449 HYPERTENSI?

L8 10 L7 AND HYPERTENSI?

=> d 18 1-10 ibib ed abs

L8 ANSWER 1 OF 10 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2005:120761 CAPLUS

TITLE: soluble guanylate cyclase activator and ACE-inhibitor
for the treatment of cardiovascular or metabolic
disorders

INVENTOR(S): Fox, David Nathan Abraham; Karran, Eric
Howard

PATENT ASSIGNEE(S): Pfizer Limited, UK; Pfizer Inc.

SOURCE: PCT Int. Appl., 27 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005011727	A1	20050210	WO 2004-IB2469	20040726
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			

PRIORITY APPLN. INFO.:

GB 2003-18094

A 20030801

ED Entered STN: 11 Feb 2005

AB The invention discloses combinations comprising (a) an activator of soluble guanylate cyclase and (b) an inhibitor of angiotensin converting enzyme (ACE) for treating a cardiovascular or metabolic disorder, in particular **hypertension** or diabetes.

REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 2 OF 10 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2005:101573 CAPLUS

TITLE: Hemodynamic effects of phosphodiesterase 5 and
angiotensin-converting enzyme inhibition alone or in
combination in conscious SHR

AUTHOR(S): Gardiner, S. M.; March, J. E.; Kemp, P. A.; Ballard, S. A.; Hawkeswood, E.; Hughes, B.; Bennett, T.

CORPORATE SOURCE: Centre for Integrated Systems Biology & Medicine, School of Biomedical Sciences, Queen's Medical Centre, University of Nottingham Medical School, Nottingham, UK

SOURCE: Journal of Pharmacology and Experimental Therapeutics (2005), 312(1), 265-271
CODEN: JPETAB; ISSN: 0022-3565

PUBLISHER: American Society for Pharmacology and Experimental Therapeutics

DOCUMENT TYPE: Journal

LANGUAGE: English

ED Entered STN: 07 Feb 2005

AB The regional hemodynamic responses to continuous 4-day infusion of UK-357,903 [1-ethyl-4-{3-[3-ethyl-6,7-dihydro-7-oxo-2-(2-pyridylmethyl)-2H-pyrazolo[4,3-d]pyrimidin-5-yl]-2-(2-methoxyethoxy)-5-pyridylsulfonyl}piperazine] (266 µg kg⁻¹ h⁻¹) alone and in combination with a low dose of enalapril (10 µg kg⁻¹ h⁻¹) were measured in conscious spontaneously **hypertensive** rats to test the hypothesis that the renin-angiotensin system may influence the cardiovascular consequences of inhibition of phosphodiesterase 5 (PDE5) by UK-357,903 or vice versa. UK-357,903 alone caused a fall in mean blood pressure (-12.1 mm Hg) associated with vasodilatation in the mesenteric and hindquarters vascular beds. The only way in which the effects of enalapril given alone differed significantly from those of the vehicle was in causing mesenteric vasodilatation, which developed over the 4 days of infusion. UK-357,903 given in combination with enalapril caused hypotension (-17.8 mm Hg) and vasodilatation in the renal, mesenteric, and hindquarter vascular beds. There was evidence of a significant interaction between the effects of the two compds. on renal Doppler shift and vascular conductance with the combined action of the two compds. being greater than the sum of their individual effects. However, although there was a trend for the combination to have greater effects than either of the individual agents on blood pressure and mesenteric vascular conductance, there was no statistical evidence of an interaction. The results indicate that inhibition of the renin-angiotensin system uncovers addnl. renal vasodilator effects of UK-357,903, and/or inhibition of PDE5 enhances the renal vasodilator effects of angiotensin-converting enzyme inhibition.

REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 3 OF 10 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:965255 CAPLUS

DOCUMENT NUMBER: 141:410950

TITLE: Preparation of 5,7-diaminopyrazolo[4,3-d]pyrimidines as selective PDE5 inhibitors useful in the treatment of **hypertension**

INVENTOR(S): Bell, Andrew Simon; Brown, David Graham; Fox, David Nathan Abraham; Marsh, Ian Roger; Morrell, Andrew Ian; Palmer, Michael John; Winslow, Carol Ann

PATENT ASSIGNEE(S): Pfizer Limited, UK; Pfizer Inc.

SOURCE: PCT Int. Appl., 279 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004096810	A1	20041111	WO 2004-IB1433	20040422
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,				

CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
 RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

NL 1026074 A1 20041101 NL 2004-1026074 20040428
 US 2005043325 A1 20050224 US 2004-834484 20040429
 PRIORITY APPLN. INFO.: GB 2003-9780 A 20030429
 GB 2003-27748 A 20031128
 US 2003-476678P P 20030606
 US 2004-538147P P 20040120

OTHER SOURCE(S): MARPAT 141:410950
 ED Entered STN: 12 Nov 2004
 GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. I [wherein R1 = (un)substituted cycloalkyl, cycloalkenyl, (un)substituted pyridin-2-yl, (un)fused Ph, etc.; R2 = H, alkyl; R3, R4 = independently (un)substituted alkyl, alkenyl, cycloalkyl, etc.; or NR3R4 = piperazin-1-yl, monocyclic, saturated polycyclic; R5 = (un)substituted halo/alkyl, alkenyl, alkynyl, cycloalkyl; R6 = H, (un)substituted alkyl, haloalkyl, alkenyl, alkynyl, etc.] were prepared as selective PDE5 inhibitors. For example, II•2HCl was prepared from (4-Methylpyridin-2-yl)amine, dichloride III (general preparation given), and tert-Bu piperazine-1-carboxylate. I gave IC50 values < 10,000 nM in an in vitro assay for PDE5 inhibition. Thus, I are used for treating **hypertension**.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 4 OF 10 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:152690 CAPLUS

DOCUMENT NUMBER: 140:332158

TITLE: Haemodynamic effects of the selective phosphodiesterase 5 inhibitor, UK-357,903, in conscious SHR

AUTHOR(S): Gardiner, Sheila M.; March, Julie E.; Kemp, Philip A.; Ballard, Stephen A.; Hawkeswood, Ed; Hughes, Bernadette; Bennett, Terence

CORPORATE SOURCE: Centre for Integrated Systems Biology & Medicine, School of Biomedical Sciences, Queen's Medical Centre, University of Nottingham Medical School, Nottingham, NG7 2UH, UK

SOURCE: British Journal of Pharmacology (2004), 141(1), 114-122

CODEN: BJPCBM; ISSN: 0007-1188

PUBLISHER: Nature Publishing Group

DOCUMENT TYPE: Journal

LANGUAGE: English

ED Entered STN: 25 Feb 2004

AB 1 Regional haemodynamic responses to a continuous, 4-day infusion of the selective phosphodiesterase type 5 inhibitor, UK-357,903 (0.133 or 1.33 mg kg⁻¹ h⁻¹) were measured in conscious spontaneously **hypertensive** rats, and compared with those of enalapril (1 mg kg⁻¹ h⁻¹). 2 Both doses of UK-357,903 caused modest redns. in mean blood pressure that were not

dose-dependent and only significantly different from the vehicle effects on Day 1 of the study (mean -11.8 and -15.3 mmHg for low and high doses, resp.). UK-357,903 had mesenteric and hindquarters vasodilator effects, which were, again, similar for both dose levels and only significantly different from vehicle on Day 1. Neither dose of UK-357,903 affected renal vascular conductance or heart rate. 3 Although the haemodynamic effects of UK-357,903 were not clearly dose-related and some appeared to wane with time, geometric mean plasma levels of UK-357,903 increased in proportion to dose, and were sustained throughout the infusion period. Furthermore, plasma cGMP, a biomarker of phosphodiesterase 5 inhibition, was persistently elevated, and increased with increasing dose. 4 Enalapril caused a fall in mean blood pressure on day 1 (-14.1 mmHg) that was associated with dilatation in renal, mesenteric and hindquarters vascular beds. The haemodynamic effects of enalapril were sustained or increased over the 4-day infusion, although plasma free drug levels were stable. 5 In conclusion, we have shown regional and temporal changes in the haemodynamic effects of UK-357,903, which may be due to activation of compensatory mechanisms, but there were no signs of functional compensation to the cardiovascular effects of enalapril.

REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 5 OF 10 CAPLUS COPYRIGHT 2005 ACS on STN
 ACCESSION NUMBER: 2004:20474 CAPLUS
 DOCUMENT NUMBER: 140:71026
 TITLE: Novel combination for treating hypertension
 INVENTOR(S): Fox, David Nathan Abraham; Hughes, Bernadette
 PATENT ASSIGNEE(S): Pfizer, Limited, UK; Pfizer, Inc.
 SOURCE: PCT Int. Appl., 25 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004002461	A2	20040108	WO 2003-IB2657	20030616
WO 2004002461	A3	20040513		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2004132731	A1	20040708	US 2003-603369	20030625
PRIORITY APPLN. INFO.:			GB 2002-14784	A 20020626
			US 2002-396780P	P 20020717

ED Entered STN: 11 Jan 2004
 AB Combinations comprising a) an inhibitor of cyclic guanosine monophosphate (cGMP) specific phosphodiesterase type 5 (PDE5) and b) an angiotensin II receptor antagonist are useful for treating hypertension. In the example provided the combined effect in hypertensive rats of candesartan and a PDE5 inhibitor was significantly larger than the sum of the 2 individual effects.

L8 ANSWER 6 OF 10 CAPLUS COPYRIGHT 2005 ACS on STN
 ACCESSION NUMBER: 2003:950772 CAPLUS
 DOCUMENT NUMBER: 140:747

TITLE: Phosphodiesterase 5 inhibitor-ACE inhibitor combination for the treatment of **hypertension**
INVENTOR(S): **Fox, David Nathan Abraham; Hughes, Bernadette**
PATENT ASSIGNEE(S): Pfizer Limited, UK; Pfizer Inc.
SOURCE: PCT Int. Appl., 25 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003099194	A2	20031204	WO 2003-IB1889	20030509
WO 2003099194	A3	20040603		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
EP 1506015	A2	20050216	EP 2003-719042	20030509
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK			
US 2004077624	A1	20040422	US 2003-443462	20030522
PRIORITY APPLN. INFO.:			GB 2002-11919	A 20020523
			GB 2002-29784	A 20021220
			US 2002-393418P	P 20020702
			US 2003-440206P	P 20030114
			WO 2003-IB1889	W 20030509

ED Entered STN: 07 Dec 2003

AB The invention discloses combinations comprising (a) an inhibitor of cyclic guanosine monophosphate (cGMP)-specific phosphodiesterase type 5 (PDE5) inhibitor and (b) an inhibitor of angiotensin converting enzyme (ACE) for treating **hypertension**.

L8 ANSWER 7 OF 10 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2003:356451 CAPLUS

DOCUMENT NUMBER: 138:368907

TITLE: Preparation of pyrazolo[4,3-d]pyrimidin-7-ones as PDE9 inhibitors for treating cardiovascular disorders

INVENTOR(S): Deninno, Michael Paul; **Hughes, Bernadette**; Kemp, Mark Ian; Palmer, Michael John; Wood, Anthony

PATENT ASSIGNEE(S): Pfizer Limited, UK; Pfizer Inc.

SOURCE: PCT Int. Appl., 69 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

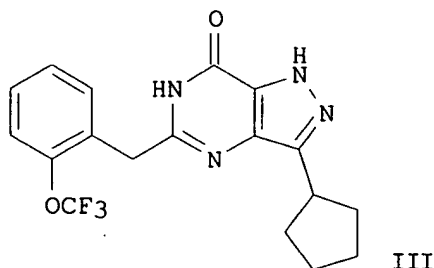
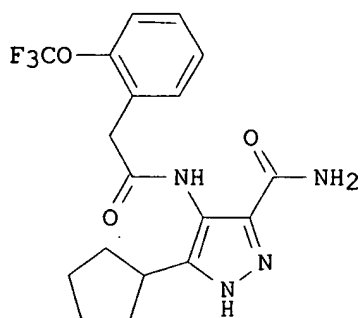
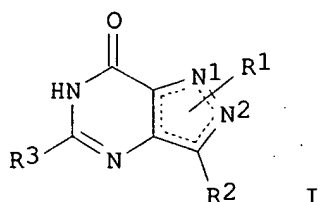
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003037899	A1	20030508	WO 2002-IB4385	20021022
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,			

UA, UG, US, UZ, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF,
CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
EP 1440073 A1 20040728 EP 2002-777623 20021022
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK
BR 2002014096 A 20040928 BR 2002-14096 20021022
US 2003195205 A1 20031016 US 2002-283514 20021030
PRIORITY APPLN. INFO.: GB 2001-26395 A 20011102
GB 2001-30695 A 20011221
GB 2002-16761 A 20020718
US 2002-350777P P 20020122
US 2002-399905P P 20020730
WO 2002-IB4385 W 20021022

OTHER SOURCE(S): MARPAT 138:368907
ED Entered STN: 09 May 2003
GI



AB The title compds. [I; R1 = H, alkyl, wherein R1 is attached to either N1 or N2; R2 = alkyl, hydroxyalkyl, alkoxyalkyl, cycloalkyl, etc.; R3 = alkyl optionally substituted by (un)substituted Ph, cycloalkyl optionally substituted by alkyl, etc.], useful as PDE9 inhibitors for treating cardiovascular disorders, were prepared and formulated. Thus, cyclization of the pyrazolecarboxamide II in the presence of tert-BuOK in iso-PrOH afforded III which was found to have a greater than 40% inhibition against PDE9 at 1 μ M.

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 8 OF 10 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1991:241037 CAPLUS

DOCUMENT NUMBER: 114:241037

TITLE: Hemodynamic effects of human α -calcitonin gene-related peptide following administration of endothelin-1 or NG-nitro-L-arginine methyl ester in conscious rats

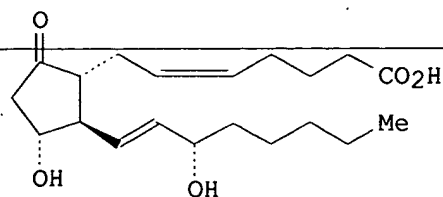
AUTHOR(S): Gardiner, S. M.; Compton, A. M.; Kemp, P. A.; Bennett, T.; Foulkes, R.; Hughes, B.
CORPORATE SOURCE: Med. Sch., Queen's Med. Cent., Nottingham, NG7 2UH, UK
SOURCE: British Journal of Pharmacology (1991), 103(1), 1256-62
CODEN: BJPCBM; ISSN: 0007-1188
DOCUMENT TYPE: Journal
LANGUAGE: English

ED Entered STN: 28 Jun 1991

AB The peripheral hemodynamic effects of human α -calcitonin gene-related peptide (α -CGRP) were studied following administration of endothelin-1 or NG-nitro-L-arginine Me ester (L-NAME), an inhibitor of nitric oxide production, in conscious, chronically-instrumented, Long Evans rats. Infusion of endothelin-1 (3 nmol/kg/h) caused **hypertension**, bradycardia and renal, mesenteric and hindquarters vasoconstrictions. Co-infusion of human α -CGRP (1.5 nmol/kg/h) reduced the **hypertension** and abolished the hindquarters vasoconstriction caused by endothelin-1, but the renal and mesenteric vasoconstrictor actions of endothelin-1 were not affected. Infusion of human α -CGRP (15 nmol/kg/h) in the presence of endothelin-1 caused hypotension and hyperemic vasodilation in the hindquarters; the mesenteric vasoconstrictor effects of endothelin-1 were diminished, but there was only a transient reversal of the renal vasoconstrictor effects of endothelin-1. Pretreatment with the nonpeptide angiotensin II receptor antagonist, DuP 753 (10 mg/kg), caused slight hypotension associated with renal, mesenteric and hindquarters vasodilations, but DuP 753 did not affect responses to endothelin-1 infusion. However, under these conditions coinfusion of human α -CGRP (15 nmol/kg/h) caused a sustained reversal of the renal vasoconstrictor effects of endothelin-1. These results indicate that the failure of human α -CGRP to cause sustained reversal of the renal vasoconstrictor effects of endothelin-1 in the absence of DuP 753 was due to activation of the renin-angiotensin system (possibly as a consequence of the hypotension). In the second experiment, L-NAME (10 mg/kg) caused renal, mesenteric and hindquarters vasoconstrictions similar to those seen in the presence of endothelin-1. However, the renal vasoconstrictor effects of L-NAME were reversed completely by human α -CGRP (15 nmol/kg/h), even though the latter caused hypotension comparable to that seen in the presence of endothelin-1. These results are consistent with a lack of functional activation of the renin-angiotensin system by human α -CGRP in the presence of L-NAME. The vasoconstrictor effects of L-NAME on the hindquarters were completely reversed by infusion of human α -CGRP, but hindquarters flow and vascular conductance did not rise above baseline levels. These results indicate the hindquarters hyperemic vasodilator effects of human α -CGRP seen in the presence of endothelin-1 were contributed to by the nitric oxide-mediated mechanisms.

L8 ANSWER 9 OF 10 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1983:193058 CAPLUS
DOCUMENT NUMBER: 98:193058
TITLE: The release of prostanoids during the acute pulmonary response to E. coli endotoxin in anesthetized cats
AUTHOR(S): Coker, Susan J.; Hughes, Bernadette; Parratt, J. R.; Rodger, I. W.; Zeitlin, I. J.
CORPORATE SOURCE: Dep. Physiol. Pharmacol., Univ. Strathclyde, Glasgow, G1 1XW, UK
SOURCE: British Journal of Pharmacology (1983), 78(3), 561-70
CODEN: BJPCBM; ISSN: 0007-1188
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 12 May 1984
GI



AB The administration of *Escherichia coli* endotoxin (2 mg/kg, i.v.) to anesthetized cats results in a characteristic acute pulmonary response. This consists of increases in pulmonary artery pressure and airways resistance and a reduction in lung compliance. Plasma concns. of PGE2 (I) [363-24-6], PGF2α [551-11-1], thromboxane B2 [54397-85-2] and 6-keto PGF1α [58962-34-8] were measured by radioimmunoassay in aortic and pulmonary arterial blood samples before, during and after the acute pulmonary response to endotoxin. Endotoxin administration resulted in the rapid release of PGF2α and thromboxane B2 from the lungs. The time course of this release was parallel to that of the pulmonary **hypertensive** and airways responses to endotoxin. PGE2 and 6-keto-PGF1α were released more gradually and with greater variations between individual animals. During the delayed shock phase (2 h after endotoxin) the concns. of PGE2, PGF2α and 6-keto PGF1α were once again elevated in both the aorta and pulmonary artery. Thromboxane B2 concns. were not increased at this time. Thus, PGF2α and thromboxane A2 may be mediators of the acute pulmonary responses to endotoxin.

L8 ANSWER 10 OF 10 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1982:137525 CAPLUS

DOCUMENT NUMBER: 96:137525

TITLE: Polymyxin B sulfate protects cats against the hemodynamic and metabolic effects of *E. coli* endotoxin
AUTHOR(S): Hughes, Bernadette; Madan, B. R.; Parratt, J. R.

CORPORATE SOURCE: Dep. Physiol. Pharmacol., Univ. Strathclyde, Glasgow, G1 1XW, UK

SOURCE: British Journal of Pharmacology (1981), 74(3), 701-7
CODEN: BJPCBM; ISSN: 0007-1188

DOCUMENT TYPE: Journal

LANGUAGE: English

ED Entered STN: 12 May 1984

AB polymyxin B sulfate (I) [1405-20-5] given i.v. 1 min before *Escherichia coli* endotoxin (2 mg/kg, i.v.) as a bolus injection (5 mg/kg) followed by a continuous i.v. infusion (addnl. 5 mg/kg given over a 30 min period) prevented the endotoxin-induced pulmonary (right atrial) **hypertension** but not the acute systemic **hypertension** in anesthetized cats. I reduced the delayed hemodynamic effects of endotoxin (systemic hypotension, decrease in cardiac output), but did not prevent the initial (1-3 h) and marked metabolic acidosis, although after 3 h arterial lactate levels returned towards control levels, whereas in the endotoxin-only group they continued to increase until death. The mechanism of this marked protective effect and the possible clin. repercussions are discussed; the most likely explanation for the protection is in chemical combination with the lipid A moiety of the endotoxin.

=> d his

(FILE 'HOME' ENTERED AT 11:49:08 ON 02 MAR 2005)

FILE 'CAPLUS' ENTERED AT 11:49:13 ON 02 MAR 2005

		E FOX DAVID/AU
L1	69	S E2-E3, E20-E22
		E HUGHES BERNADETTE/AU
L2	22	S E3-E4
		E HUGHES B/AU
L3	40	S E3
		E FOX D/AU
		E FOX D?/AU
		E FOX D/AU
L4	75	S E3
L5	144	S L1 OR L4
L6	62	S L2 OR L3
L7	204	S L5 OR L6
L8	10	S L7 AND HYPERTENSI?

=> s l7 and (cyclic guanosine monophosphate (w) (phosphodiesterase or "PDE5")) and (angiotensin)

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286246 CYCLIC
330 CYCLICS
286374 CYCLIC
      (CYCLIC OR CYCLICS)
21456 GUANOSINE
313 GUANOSINES
21565 GUANOSINE
      (GUANOSINE OR GUANOSINES)
29181 MONOPHOSPHATE
3848 MONOPHOSPHATES
31896 MONOPHOSPHATE
      (MONOPHOSPHATE OR MONOPHOSPHATES)
835 CYCLIC GUANOSINE MONOPHOSPHATE
      (CYCLIC(W) GUANOSINE(W) MONOPHOSPHATE)
24057 PHOSPHODIESTERASE
2560 PHOSPHODIESTERASES
24563 PHOSPHODIESTERASE
      (PHOSPHODIESTERASE OR PHOSPHODIESTERASES)
533 "PDE5"
35 CYCLIC GUANOSINE MONOPHOSPHATE (W) (PHOSPHODIESTERASE OR "PDE5")
54762 ANGIOTENSIN
1691 ANGIOTENSINS
54850 ANGIOTENSIN
      (ANGIOTENSIN OR ANGIOTENSINS)
L9      0 L7 AND (CYCLIC GUANOSINE MONOPHOSPHATE (W) (PHOSPHODIESTERASE
      OR "PDE5")) AND (ANGIOTENSIN)

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=> s l7 and ("cgmp" or "pde5" or "angiotensin II receptor antagonist")

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20057 "CGMP"
187 "CGMPS"
20081 "CGMP"
      ("CGMP" OR "CGMPS")
533 "PDE5"
54762 "ANGIOTENSIN"
1691 "ANGIOTENSINS"
54850 "ANGIOTENSIN"
      ("ANGIOTENSIN" OR "ANGIOTENSINS")
2015064 "II"
825 "IIS"
2015534 "II"
      ("II" OR "IIS")
591069 "RECEPTOR"
542204 "RECEPTORS"
703691 "RECEPTOR"
      ("RECEPTOR" OR "RECEPTORS")
149224 "ANTAGONIST"
108335 "ANTAGONISTS"

```

200876 "ANTAGONIST"

("ANTAGONIST" OR "ANTAGONISTS")

1675 "ANGIOTENSIN II RECEPTOR ANTAGONIST"

("ANGIOTENSIN" (W) "II" (W) "RECEPTOR" (W) "ANTAGONIST")

L10 6 L7 AND ("CGMP" OR "PDE5" OR "ANGIOTENSIN II RECEPTOR ANTAGONIST")

=> d l10 1-6 ibib ed abs

L10 ANSWER 1 OF 6 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2005:101573 CAPLUS

TITLE: Hemodynamic effects of phosphodiesterase 5 and angiotensin-converting enzyme inhibition alone or in combination in conscious SHR

AUTHOR(S): Gardiner, S. M.; March, J. E.; Kemp, P. A.; Ballard, S. A.; Hawkeswood, E.; Hughes, B.; Bennett, T.

CORPORATE SOURCE: Centre for Integrated Systems Biology & Medicine, School of Biomedical Sciences, Queen's Medical Centre, University of Nottingham Medical School, Nottingham, UK

SOURCE: Journal of Pharmacology and Experimental Therapeutics (2005), 312(1), 265-271

CODEN: JPETAB; ISSN: 0022-3565

PUBLISHER: American Society for Pharmacology and Experimental Therapeutics

DOCUMENT TYPE: Journal

LANGUAGE: English

ED Entered STN: 07 Feb 2005

AB The regional hemodynamic responses to continuous 4-day infusion of UK-357,903 [1-ethyl-4-{3-[3-ethyl-6,7-dihydro-7-oxo-2-(2-pyridylmethyl)-2H-pyrazolo[4,3-d]pyrimidin-5-yl]-2-(2-methoxyethoxy)-5-pyridylsulfonyl}piperazine] (266 µg kg⁻¹ h⁻¹) alone and in combination with a low dose of enalapril (10 µg kg⁻¹ h⁻¹) were measured in conscious spontaneously hypertensive rats to test the hypothesis that the renin-angiotensin system may influence the cardiovascular consequences of inhibition of phosphodiesterase 5 (PDE5) by UK-357,903 or vice versa. UK-357,903 alone caused a fall in mean blood pressure (-12.1 mm Hg) associated with vasodilatation in the mesenteric and hindquarters vascular beds. The only way in which the effects of enalapril given alone differed significantly from those of the vehicle was in causing mesenteric vasodilatation, which developed over the 4 days of infusion. UK-357,903 given in combination with enalapril caused hypotension (-17.8 mm Hg) and vasodilatation in the renal, mesenteric, and hindquarter vascular beds. There was evidence of a significant interaction between the effects of the two compds. on renal Doppler shift and vascular conductance with the combined action of the two compds. being greater than the sum of their individual effects. However, although there was a trend for the combination to have greater effects than either of the individual agents on blood pressure and mesenteric vascular conductance, there was no statistical evidence of an interaction. The results indicate that inhibition of the renin-angiotensin system uncovers addnl. renal vasodilator effects of UK-357,903, and/or inhibition of PDE5 enhances the renal vasodilator effects of angiotensin-converting enzyme inhibition.

REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:965255 CAPLUS

DOCUMENT NUMBER: 141:410950

TITLE: Preparation of 5,7-diaminopyrazolo[4,3-d]pyrimidines as selective PDE5 inhibitors useful in the treatment of hypertension

INVENTOR(S): Bell, Andrew Simon; Brown, David Graham; **Fox,**
David Nathan Abraham; Marsh, Ian Roger; Morrell,
 Andrew Ian; Palmer, Michael John; Winslow, Carol Ann
 PATENT ASSIGNEE(S): Pfizer Limited, UK; Pfizer Inc.
 SOURCE: PCT Int. Appl., 279 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004096810	A1	20041111	WO 2004-IB1433	20040422
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
NL 1026074	A1	20041101	NL 2004-1026074	20040428
US 2005043325	A1	20050224	US 2004-834484	20040429
PRIORITY APPLN. INFO.:			GB 2003-9780	A 20030429
			GB 2003-27748	A 20031128
			US 2003-476678P	P 20030606
			US 2004-538147P	P 20040120

OTHER SOURCE(S): MARPAT 141:410950
 ED Entered STN: 12 Nov 2004
 GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. I [wherein R1 = (un)substituted cycloalkyl, cycloalkenyl, (un)substituted pyridin-2-yl, (un)fused Ph, etc.; R2 = H, alkyl; R3, R4 = independently (un)substituted alkyl, alkenyl, cycloalkyl, etc.; or NR3R4 = piperazin-1-yl, monocyclic, saturated polycyclic; R5 = (un)substituted halo/alkyl, alkenyl, alkynyl, cycloalkyl; R6 = H, (un)substituted alkyl, haloalkyl, alkenyl, alkynyl, etc.] were prepared as selective **PDE5** inhibitors. For example, II•2HCl was prepared from (4-Methylpyridin-2-yl)amine, dichloride III (general preparation given), and tert-Bu piperazine-1-carboxylate. I gave IC50 values < 10,000 nM in an in vitro assay for **PDE5** inhibition. Thus, I are used for treating hypertension.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:152690 CAPLUS

DOCUMENT NUMBER: 140:332158

TITLE: Haemodynamic effects of the selective phosphodiesterase 5 inhibitor, UK-357,903, in conscious SHR

AUTHOR(S): Gardiner, Sheila M.; March, Julie E.; Kemp, Philip A.; Ballard, Stephen A.; Hawkeswood, Ed; **Hughes,**
Bernadette; Bennett, Terence

CORPORATE SOURCE: Centre for Integrated Systems Biology & Medicine,

School of Biomedical Sciences, Queen's Medical Centre,
University of Nottingham Medical School, Nottingham,
NG7 2UH, UK

SOURCE: British Journal of Pharmacology (2004), 141(1),
114-122

CODEN: BJPCBM; ISSN: 0007-1188

PUBLISHER: Nature Publishing Group

DOCUMENT TYPE: Journal

LANGUAGE: English

ED Entered STN: 25 Feb 2004

AB 1 Regional haemodynamic responses to a continuous, 4-day infusion of the selective phosphodiesterase type 5 inhibitor, UK-357,903 (0.133 or 1.33 mg kg⁻¹ h⁻¹) were measured in conscious spontaneously hypertensive rats, and compared with those of enalapril (1 mg kg⁻¹ h⁻¹). 2 Both doses of UK-357,903 caused modest redns. in mean blood pressure that were not dose-dependent and only significantly different from the vehicle effects on Day 1 of the study (mean -11.8 and -15.3 mmHg for low and high doses, resp.). UK-357,903 had mesenteric and hindquarters vasodilator effects, which were, again, similar for both dose levels and only significantly different from vehicle on Day 1. Neither dose of UK-357,903 affected renal vascular conductance or heart rate. 3 Although the haemodynamic effects of UK-357,903 were not clearly dose-related and some appeared to wane with time, geometric mean plasma levels of UK-357,903 increased in proportion to dose, and were sustained throughout the infusion period. Furthermore, plasma **cgmp**, a biomarker of phosphodiesterase 5 inhibition, was persistently elevated, and increased with increasing dose. 4 Enalapril caused a fall in mean blood pressure on day 1 (-14.1 mmHg) that was associated with dilatation in renal, mesenteric and hindquarters vascular beds. The haemodynamic effects of enalapril were sustained or increased over the 4-day infusion, although plasma free drug levels were stable. 5 In conclusion, we have shown regional and temporal changes in the haemodynamic effects of UK-357,903, which may be due to activation of compensatory mechanisms, but there were no signs of functional compensation to the cardiovascular effects of enalapril.

REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:20474 CAPLUS

DOCUMENT NUMBER: 140:71026

TITLE: Novel combination for treating hypertension

INVENTOR(S): **Fox, David Nathan Abraham; Hughes, Bernadette**

PATENT ASSIGNEE(S): Pfizer, Limited, UK; Pfizer, Inc.

SOURCE: PCT Int. Appl., 25 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004002461	A2	20040108	WO 2003-IB2657	20030616
WO 2004002461	A3	20040513		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,			

BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
 US 2004132731 A1 20040708 US 2003-603369 20030625

PRIORITY APPLN. INFO.: GB 2002-14784 A 20020626
 US 2002-396780P P 20020717

ED Entered STN: 11 Jan 2004
 AB Combinations comprising a) an inhibitor of cyclic guanosine monophosphate (cGMP) specific phosphodiesterase type 5 (PDE5) and b) an angiotensin II receptor antagonist are useful for treating hypertension. In the example provided the combined effect in hypertensive rats of candesartan and a PDE5 inhibitor was significantly larger than the sum of the 2 individual effects.

L10 ANSWER 5 OF 6 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2003:950772 CAPLUS
 DOCUMENT NUMBER: 140:747
 TITLE: Phosphodiesterase 5 inhibitor-ACE inhibitor combination for the treatment of hypertension
 INVENTOR(S): Fox, David Nathan Abraham; Hughes, Bernadette
 PATENT ASSIGNEE(S): Pfizer Limited, UK; Pfizer Inc.
 SOURCE: PCT Int. Appl., 25 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003099194	A2	20031204	WO 2003-IB1889	20030509
WO 2003099194	A3	20040603		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
EP 1506015	A2	20050216	EP 2003-719042	20030509
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK			
US 2004077624	A1	20040422	US 2003-443462	20030522
PRIORITY APPLN. INFO.:			GB 2002-11919	A 20020523
			GB 2002-29784	A 20021220
			US 2002-393418P	P 20020702
			US 2003-440206P	P 20030114
			WO 2003-IB1889	W 20030509

ED Entered STN: 07 Dec 2003
 AB The invention discloses combinations comprising (a) an inhibitor of cyclic guanosine monophosphate (cGMP)-specific phosphodiesterase type 5 (PDE5) inhibitor and (b) an inhibitor of angiotensin converting enzyme (ACE) for treating hypertension.

L10 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1991:241037 CAPLUS
 DOCUMENT NUMBER: 114:241037
 TITLE: Hemodynamic effects of human α -calcitonin gene-related peptide following administration of endothelin-1 or NG-nitro-L-arginine methyl ester in conscious rats

AUTHOR(S): Gardiner, S. M.; Compton, A. M.; Kemp, P. A.; Bennett, T.; Foulkes, R.; Hughes, B.
CORPORATE SOURCE: Med. Sch., Queen's Med. Cent., Nottingham, NG7 2UH, UK
SOURCE: British Journal of Pharmacology (1991), 103(1), 1256-62
CODEN: BJPCBM; ISSN: 0007-1188
DOCUMENT TYPE: Journal
LANGUAGE: English

ED Entered STN: 28 Jun 1991

AB The peripheral hemodynamic effects of human α -calcitonin gene-related peptide (α -CGRP) were studied following administration of endothelin-1 or NG-nitro-L-arginine Me ester (L-NAME), an inhibitor of nitric oxide production, in conscious, chronically-instrumented, Long Evans rats. Infusion of endothelin-1 (3 nmol/kg/h) caused hypertension, bradycardia and renal, mesenteric and hindquarters vasoconstrictions. Co-infusion of human α -CGRP (1.5 nmol/kg/h) reduced the hypertension and abolished the hindquarters vasoconstriction caused by endothelin-1, but the renal and mesenteric vasoconstrictor actions of endothelin-1 were not affected. Infusion of human α -CGRP (15 nmol/kg/h) in the presence of endothelin-1 caused hypotension and hyperemic vasodilation in the hindquarters; the mesenteric vasoconstrictor effects of endothelin-1 were diminished, but there was only a transient reversal of the renal vasoconstrictor effects of endothelin-1. Pretreatment with the nonpeptide **angiotensin II receptor antagonist**, DuP 753 (10 mg/kg), caused slight hypotension associated with renal, mesenteric and hindquarters vasodilations, but DuP 753 did not affect responses to endothelin-1 infusion. However, under these conditions coinfusion of human α -CGRP (15 nmol/kg/h) caused a sustained reversal of the renal vasoconstrictor effects of endothelin-1. These results indicate that the failure of human α -CGRP to cause sustained reversal of the renal vasoconstrictor effects of endothelin-1 in the absence of DuP 753 was due to activation of the renin-angiotensin system (possibly as a consequence of the hypotension). In the second experiment, L-NAME (10 mg/kg) caused renal, mesenteric and hindquarters vasoconstrictions similar to those seen in the presence of endothelin-1. However, the renal vasoconstrictor effects of L-NAME were reversed completely by human α -CGRP (15 nmol/kg/h), even though the latter caused hypotension comparable to that seen in the presence of endothelin-1. These results are consistent with a lack of functional activation of the renin-angiotensin system by human α -CGRP in the presence of L-NAME. The vasoconstrictor effects of L-NAME on the hindquarters were completely reversed by infusion of human α -CGRP, but hindquarters flow and vascular conductance did not rise above baseline levels. These results indicate the hindquarters hyperemic vasodilator effects of human α -CGRP seen in the presence of endothelin-1 were contributed to by the nitric oxide-mediated mechanisms.

=> d cost

COST IN U.S. DOLLARS	SINCE FILE	TOTAL
	ENTRY	SESSION
CONNECT CHARGES	5.46	5.61
NETWORK CHARGES	0.84	0.90
SEARCH CHARGES	41.58	41.58
DISPLAY CHARGES	42.40	42.40
	-----	-----
FULL ESTIMATED COST	90.28	90.49
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE	TOTAL
	ENTRY	SESSION
CA SUBSCRIBER PRICE	-11.68	-11.68

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=> d his

(FILE 'HOME' ENTERED AT 11:49:08 ON 02 MAR 2005)

FILE 'CAPLUS' ENTERED AT 11:49:13 ON 02 MAR 2005

E FOX DAVID/AU
L1 69 S E2-E3, E20-E22
E HUGHES BERNADETTE/AU
L2 22 S E3-E4
E HUGHES B/AU
L3 40 S E3
E FOX D/AU
E FOX D?/AU
E FOX D/AU
L4 75 S E3
L5 144 S L1 OR L4
L6 62 S L2 OR L3
L7 204 S L5 OR L6
L8 10 S L7 AND HYPERTENSI?
L9 0 S L7 AND (CYCLIC GUANOSINE MONOPHOSPHATE (W) (PHOSPHODIESTERASE
L10 6 S L7 AND ("CGMP" OR "PDE5" OR "ANGIOTENSIN II RECEPTOR ANTAGONI

=> file registry

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	90.28	90.49
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-11.68	-11.68

FILE 'REGISTRY' ENTERED AT 11:57:43 ON 02 MAR 2005

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DICTIONARY FILE UPDATES: 1 MAR 2005 HIGHEST RN 840454-17-3

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<http://www.cas.org/ONLINE/DBSS/registryss.html>

=> e sildenafil/cn

E1 1 SILD (STREPTOCOCCUS PYOGENES GENE SILD)/CN
E2 1 SILDATE/CN
E3 1 --> SILDENAFIL/CN
E4 1 SILDENAFIL CITRATE/CN
E5 1 SILDENAFIL MALEATE/CN
E6 1 SILDENAFIL MONOMALEATE/CN
E7 1 SILDENAFIL NITRATE/CN
E8 1 SILDEX/CN

```
E9      1      SILDEX C 303/CN
E10     1      SILDEX H 121/CN
E11     1      SILDEX H 32/CN
E12     1      SILDEX H 51/CN
```

=> s e3-e4

```
      1 SILDENAFIL/CN
      1 "SILDENAFIL CITRATE"/CN
L11     2 (SILDENAFIL/CN OR "SILDENAFIL CITRATE"/CN)
```

=> e tadalafil/an

'AN' IS NOT A VALID EXPAND FIELD CODE FOR FILE 'REGISTRY'
The indicated field code is not available for EXPAND in this
file. To see a list of valid EXPAND field codes, enter HELP
SFIELDS at an arrow prompt (=>).

=> e tadalafil/cn

```
E1      1      TADA3L PROTEIN (MOUSE STRAIN FVB/N CLONE MGC:31487 IMAGE:448
      6171)/CN
E2      1      TADAB/CN
E3      1 --> TADALAFIL/CN
E4      1      TADB/CN
E5      1      TADB (PASTEURELLA MULTOCIDA STRAIN IL1403 CLONE PM70 GENE TA
      DB)/CN
E6      1      TADB (VIBRIO PARAHAEMOLYTICUS STRAIN O3:K6 GENE VPA0725)/CN
E7      1      TADB PROTEIN (CHLOROBIMUM TEPIDUM STRAIN TLS GENE TADB)/CN
E8      1      TADB-LIKE PROTEIN (PLASMID PBD2 GENE PBD2.017)/CN
E9      1      TADC (PASTEURELLA MULTOCIDA STRAIN IL1403 CLONE PM70 GENE TA
      DC)/CN
E10     1      TADC (VIBRIO PARAHAEMOLYTICUS STRAIN O3:K6 GENE VPA0726)/CN
E11     1      TADC PROTEIN (CHLOROBIMUM TEPIDUM STRAIN TLS GENE CT0436)/CN
E12     1      TADCO ALPHA BLUE DYE/CN
```

=> s e3

```
L12     1 TADALAFIL/CN
```

=> e vardenafil/cn

```
E1      1      VARD/CN
E2      1      VARDAX/CN
E3      1 --> VARDENAFIL/CN
E4      1      VARDENAFIL DIHYDROCHLORIDE/CN
E5      1      VARDENAFIL HYDROCHLORIDE/CN
E6      1      VARDHAK/CN
E7      1      VARDHMAN/CN
E8      1      VAREBIAN/CN
E9      1      VARENICLINE/CN
E10     1      VARENICLINE TARTRATE/CN
E11     1      VARENNESITE/CN
E12     1      VARENNESITE ((MN0.5-1FE0-0.5)2NA8((OH)0.5-1CL0-0.5)2(SI2O5)5
      .12H2O)/CN
```

=> s e3-e5

```
      1 VARDENAFIL/CN
      1 "VARDENAFIL DIHYDROCHLORIDE"/CN
      1 "VARDENAFIL HYDROCHLORIDE"/CN
L13     3 (VARDENAFIL/CN OR "VARDENAFIL DIHYDROCHLORIDE"/CN OR "VARDENAFIL
      HYDROCHLORIDE"/CN)
```

=> s candesartan/cn

```
L14     1 CANDESARTAN/CN
```

=> e candesartan/cn

```
E1      1      CANDESALVONE B METHYL ESTER/CN
E2      1      CANDESALVOQUINONE/CN
```

E3	1	--> CANDESARTAN/CN
E4	1	CANDESARTAN CILEXETIL/CN
E5	1	CANDESARTAN M1/CN
E6	1	CANDEX/CN
E7	1	CANDICANDIOL/CN
E8	1	CANDICANDIOL A/CN
E9	1	CANDICANDIOL B/CN
E10	1	CANDICANDIOL DIACETATE/CN
E11	1	CANDICANIN/CN
E12	1	CANDICANIN ACETATE/CN

=> s e3-e5

	1	CANDESARTAN/CN
	1	"CANDESARTAN CILEXETIL"/CN
	1	"CANDESARTAN M1"/CN
L15	2	(CANDESARTAN/CN OR "CANDESARTAN CILEXETIL"/CN OR "CANDESARTAN M1"/CN)

=> e eprosartan/cn

E1	1	EPROLIN S/CN
E2	1	EPRONAZ/CN
E3	1	--> EPROSARTAN/CN
E4	1	EPROSARTAN MESYLATE/CN
E5	1	EPROSARTAN METHANESULFONATE/CN
E6	1	EPROSIN/CN
E7	1	EPROSIN 15/CN
E8	1	EPROSIN E 1/CN
E9	1	EPROSIN E 26/CN
E10	1	EPROSIN E 3/CN
E11	1	EPROSIN T 05/CN
E12	1	EPROSIN T 06/CN

=> s e3-e5

	1	EPROSARTAN/CN
	1	"EPROSARTAN MESYLATE"/CN
	1	"EPROSARTAN METHANESULFONATE"/CN
L16	2	(EPROSARTAN/CN OR "EPROSARTAN MESYLATE"/CN OR "EPROSARTAN METHANESULFONATE"/CN)

=> e irbesartan/cn

E1	1	IRB5 (VIBRIO CHOLERAЕ STRAIN 569B CLONE PRAP5)/CN
E2	1	IRBADAZINE/CN
E3	1	--> IRBESARTAN/CN
E4	1	IRBESARTAN METABOLITE 5/CN
E5	1	IRBESARTAN METABOLITE 7/CN
E6	1	IRBESARTAN-HYDROCHLOROTHIAZIDE MIXT./CN
E7	1	IRBP (ALLENOPITHECUS NIGROVIRIDIS STRAIN SPECIMEN-VOUCHER-R1 46/97 GENE IRBP FRAGMENT)/CN
E8	1	IRBP (CERCOPITHECUS MONA STRAIN COUNTRY-GRENADA-SPECIMEN-VOUCHER-SA.BF#3 GENE IRBP FRAGMENT)/CN
E9	1	IRBP (INTERSTITIAL RETINOL-BINDING PROTEIN) (DROSOPHILA MELANOGASTER)/CN
E10	1	IRBP (MACACA ARCTOIDES STRAIN COUNTRY-MALAYSIA-SPECIMEN-VOUCHER-101.MALAYA GENE IRBP FRAGMENT)/CN
E11	1	IRBP (MACACA ARCTOIDES STRAIN COUNTRY-VIET-NAM-SPECIMEN-VOUCHER-HANOI.05.2 GENE IRBP FRAGMENT)/CN
E12	1	IRBP (MACACA ARCTOIDES STRAIN SPECIMEN-VOUCHER-ST0316 GENE IRBP FRAGMENT)/CN

=> s e3-e6

	1	IRBESARTAN/CN
	1	"IRBESARTAN METABOLITE 5"/CN
	1	"IRBESARTAN METABOLITE 7"/CN
	1	"IRBESARTAN-HYDROCHLOROTHIAZIDE MIXT."/CN

L17 4 (IRBESARTAN/CN OR "IRBESARTAN METABOLITE 5"/CN OR "IRBESARTAN METABOLITE 7"/CN OR "IRBESARTAN-HYDROCHLOROTHIAZIDE MIXT."/CN)

=> e losartan/cn

E1	1	LOSAN/CN
E2	1	LOSANTIN/CN
E3	1	--> LOSARTAN/CN
E4	1	LOSARTAN MONOPOTASSIUM SALT/CN
E5	1	LOSARTAN P-TOLUENESULFONATE/CN
E6	1	LOSARTAN POTASSIUM/CN
E7	1	LOSARTAN-HYDROCHLOROTHIAZIDE MIXT./CN
E8	1	LOSANINE/CN
E9	1	LOSE-URONATE KETOL-ISOMERASE (YERSINIA PESTIS STRAIN CO92 GE NE KDUI)/CN
E10	1	LOSEC/CN
E11	1	LOSEC SODIUM/CN
E12	1	LOSEYITE/CN

=> s e3-e7

	1	LOSARTAN/CN
	1	"LOSARTAN MONOPOTASSIUM SALT"/CN
	1	"LOSARTAN P-TOLUENESULFONATE"/CN
	1	"LOSARTAN POTASSIUM"/CN
	1	"LOSARTAN-HYDROCHLOROTHIAZIDE MIXT."/CN
L18	4	(LOSARTAN/CN OR "LOSARTAN MONOPOTASSIUM SALT"/CN OR "LOSARTAN P-TOLUENESULFONATE"/CN OR "LOSARTAN POTASSIUM"/CN OR "LOSARTAN-HYDROCHLOROTHIAZIDE MIXT."/CN)

=> e olmesartan/cn

E1	1	OLMECOL/CN
E2	1	OLMELIN/CN
E3	1	--> OLMESARTAN/CN
E4	1	OLMESARTAN MEDOXOMIL/CN
E5	1	OLMETEC/CN
E6	1	OLMIDE/CN
E7	1	OLMIDINE/CN
E8	1	OLMIFON/CN
E9	1	OLMSTEADITE/CN
E10	1	OLN 4/CN
E11	1	OLN 50/CN
E12	1	OLN-1/CN

=> s e3-e5

	1	OLMESARTAN/CN
	1	"OLMESARTAN MEDOXOMIL"/CN
	1	OLMETEC/CN
L19	2	(OLMESARTAN/CN OR "OLMESARTAN MEDOXOMIL"/CN OR OLMETEC/CN)

=> e saralasin/cn

E1	1	SARALINE C ACETATE/CN
E2	1	SARAKALIM/CN
E3	1	--> SARALASIN/CN
E4	1	SARALASIN ACETATE/CN
E5	1	SARALINE 200/CN
E6	1	SARALINK 545/CN
E7	1	SARAMET/CN
E8	1	SARAMIN/CN
E9	1	SARAMYCETIC ACID/CN
E10	1	SARAMYCETIC ACID A/CN
E11	1	SARAMYCETIN/CN
E12	1	SARAMYCETOIC ACID/CN

=> s e3-e4

	1	SARALASIN/CN
--	---	--------------

L20 1 "SARALASIN ACETATE"/CN
2 (SARALASIN/CN OR "SARALASIN ACETATE"/CN)

=> e telmisartan/cn

E1 1 TELMIN B/CN
E2 1 TELMION/CN
E3 1 --> TELMISARTAN/CN
E4 1 TELMISARTAN GLUCURONIDE/CN
E5 1 TELMISARTAN HYDROCHLORIDE/CN
E6 1 TELMISARTAN SODIUM HEMIHYDRATE/CN
E7 1 TELMISARTAN SODIUM SALT/CN
E8 1 TELO-PROPEPTIDE OF ALPHA 1 (III) PROCOLLAGEN (HUMAN)/CN
E9 1 TELOBINE/CN
E10 1 TELOCINOBUFAGIN/CN
E11 1 TELOCINOBUFAGIN 3-HEMISUBERATE/CN
E12 1 TELOCINOBUFAGIN 3-HEMISUBERATE P-NITROPHENYL ESTER/CN

=> s e3-e7

1 TELMISARTAN/CN
1 "TELMISARTAN GLUCURONIDE"/CN
1 "TELMISARTAN HYDROCHLORIDE"/CN
1 "TELMISARTAN SODIUM HEMIHYDRATE"/CN
1 "TELMISARTAN SODIUM SALT"/CN
L21 5 (TELMISARTAN/CN OR "TELMISARTAN GLUCURONIDE"/CN OR "TELMISARTAN
HYDROCHLORIDE"/CN OR "TELMISARTAN SODIUM HEMIHYDRATE"/CN OR
"TELMISARTAN SODIUM SALT"/CN)

=> e valsartan/cn

E1 1 VALSARIN/CN
E2 1 VALSARIN ACETATE/CN
E3 1 --> VALSARTAN/CN
E4 1 VALSARTAN METHYL ESTER/CN
E5 1 VALSOF PE 40/CN
E6 1 VALSOL LTA/CN
E7 1 VALSOL LTA-N/CN
E8 1 VALSPAR/CN
E9 1 VALSPAR EPS 2718/CN
E10 1 VALSPAR FBE-D 2003DV/CN
E11 1 VALSPAR S 9783-002/CN
E12 1 VALSPEX 155-53/CN

=> s e3-e4

1 VALSARTAN/CN
1 "VALSARTAN METHYL ESTER"/CN
L22 2 (VALSARTAN/CN OR "VALSARTAN METHYL ESTER"/CN)

=> d his

(FILE 'HOME' ENTERED AT 11:49:08 ON 02 MAR 2005)

FILE 'CAPLUS' ENTERED AT 11:49:13 ON 02 MAR 2005

E FOX DAVID/AU
L1 69 S E2-E3, E20-E22
E HUGHES BERNADETTE/AU
L2 22 S E3-E4
E HUGHES B/AU
L3 40 S E3
E FOX D/AU
E FOX D?/AU
E FOX D/AU
L4 75 S E3
L5 144 S L1 OR L4
L6 62 S L2 OR L3
L7 204 S L5 OR L6

L8 10 S L7 AND HYPERTENSI?
 L9 0 S L7 AND (CYCLIC GUANOSINE MONOPHOSPHATE (W) (PHOSPHODIESTERASE
 L10 6 S L7 AND ("CGMP" OR "PDE5" OR "ANGIOTENSIN II RECEPTOR ANTAGONI

FILE 'REGISTRY' ENTERED AT 11:57:43 ON 02 MAR 2005

E SILDENAFIL/CN
 L11 2 S E3-E4
 E TADALAFIL/CN
 L12 1 S E3
 E VARDENAFIL/CN
 L13 3 S E3-E5
 L14 1 S CANDESARTAN/CN
 E CANDESARTAN/CN
 L15 2 S E3-E5
 E EPROSARTAN/CN
 L16 2 S E3-E5
 E IRBESARTAN/CN
 L17 4 S E3-E6
 E LOSARTAN/CN
 L18 4 S E3-E7
 E OLMESARTAN/CN
 L19 2 S E3-E5
 E SARALASIN/CN
 L20 2 S E3-E4
 E TELMISARTAN/CN
 L21 5 S E3-E7
 E VALSARTAN/CN
 L22 2 S E3-E4

=> d: cost

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
CONNECT CHARGES	1.85	7.46
NETWORK CHARGES	0.30	1.20
SEARCH CHARGES	156.40	197.98
DISPLAY CHARGES	0.00	42.40
FULL ESTIMATED COST	158.55	249.04
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	0.00	-11.68

IN FILE 'REGISTRY' AT 12:00:50 ON 02 MAR 2005

=> s l11 or l12 or l13

L23 6 L11 OR L12 OR L13

=> s l15 or l16 or l17 or l18 or l19 or l20 or l21 or l22

L24 23 L15 OR L16 OR L17 OR L18 OR L19 OR L20 OR L21 OR L22

=> file caplus

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	159.41	249.90
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	0.00	-11.68

FILE 'CAPLUS' ENTERED AT 12:02:01 ON 02 MAR 2005

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FILE COVERS 1907 - 2 Mar 2005 VOL 142 ISS 10
FILE LAST UPDATED: 1 Mar 2005 (20050301/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s 123

L25 1081 L23

=> s 124

L26 4320 L24

=> e hypertension/bi

E1	2	HYPERTENSIO/BI
E2	3	HYPERTENSIogenic/BI
E3	70452 -->	HYPERTENSION/BI
E4	1	HYPERTENSION1/BI
E5	1	HYPERTENSION3/BI
E6	2	HYPERTENSION5/BI
E7	3	HYPERTENSIONAL/BI
E8	1	HYPERTENSIONC/BI
E9	1	HYPERTENSIONGENIC/BI
E10	1	HYPERTENSIONN/BI
E11	1	HYPERTENSIONOGENIC/BI
E12	1	HYPERTENSIONOLOGY/BI

=> e

E13	96	HYPERTENSIONS/BI
E14	1	HYPERTENSISVE/BI
E15	1	HYPERTENSIV/BI
E16	34458	HYPERTENSIVE/BI
E17	4	HYPERTENSIVELY/BI
E18	1	HYPERTENSIVEN/BI
E19	1	HYPERTENSIVENESS/BI
E20	1	HYPERTENSIVERATS/BI
E21	1927	HYPERTENSIVES/BI
E22	1	HYPERTENSIVEW/BI
E23	1	HYPERTENSIVITY/BI
E24	9	HYPERTENSOGENIC/BI

=> s e3, e16

	70452	HYPERTENSION/BI
	96	HYPERTENSIONS/BI
	70470	HYPERTENSION/BI
		((HYPERTENSION OR HYPERTENSIONS)/BI)
	34458	HYPERTENSIVE/BI
	1927	HYPERTENSIVES/BI
	35172	HYPERTENSIVE/BI
		((HYPERTENSIVE OR HYPERTENSIVES)/BI)
L27	78751	(HYPERTENSION/BI OR HYPERTENSIVE/BI)

=> e hypertension/ct

E#	FREQUENCY	AT	TERM
----	-----	--	-----
E1	1	7	HYPERTELIS/CT
E2	0	10	HYPERTENSIN/CT
E3	43383	15	--> HYPERTENSION/CT
E4	0	6	HYPERTENSION (L) BORDERLINE/CT
E5	0	6	HYPERTENSION (L) CHRONIC/CT
E6	0	6	HYPERTENSION (L) DAHL SALT-SENSITIVE/CT
E7	0	8	HYPERTENSION (L) ESSENTIAL/CT
E8	0	7	HYPERTENSION (L) GENETIC/CT
E9	0	6	HYPERTENSION (L) GOLDBLATT/CT
E10	0	2	HYPERTENSION (L) HYPOXIC PULMONARY/CT
E11	0	8	HYPERTENSION (L) INTRACRANIAL/CT
E12	0	8	HYPERTENSION (L) MALIGNANT/CT

=> e

E13	0	6	HYPERTENSION (L) MINERALOCORTICOID/CT
E14	0	13	HYPERTENSION (L) MINERALOCORTICOID SALT-SENSITIVE/CT
E15	0	7	HYPERTENSION (L) ONE-KIDNEY ONE-CLIP/CT
E16	0	7	HYPERTENSION (L) PORTAL/CT
E17	0	7	HYPERTENSION (L) PULMONARY/CT
E18	0	7	HYPERTENSION (L) PULMONARY, HYPOXIC/CT
E19	0	7	HYPERTENSION (L) RENAL/CT
E20	0	6	HYPERTENSION (L) RENOVASCULAR/CT
E21	0	6	HYPERTENSION (L) RENOVASCULAR, CHRONIC/CT
E22	0	6	HYPERTENSION (L) SALT-RESISTANT/CT
E23	0	8	HYPERTENSION (L) SALT-SENSITIVE/CT
E24	0	6	HYPERTENSION (L) SPONTANEOUS/CT

=> s e3

L28 43383 HYPERTENSION/CT

=> d his

(FILE 'HOME' ENTERED AT 11:49:08 ON 02 MAR 2005)

FILE 'CAPLUS' ENTERED AT 11:49:13 ON 02 MAR 2005

		E FOX DAVID/AU
L1	69	S E2-E3, E20-E22
		E HUGHES BERNADETTE/AU
L2	22	S E3-E4
		E HUGHES B/AU
L3	40	S E3
		E FOX D/AU
		E FOX D?/AU
		E FOX D/AU
L4	75	S E3
L5	144	S L1 OR L4
L6	62	S L2 OR L3
L7	204	S L5 OR L6
L8	10	S L7 AND HYPERTENSI?
L9	0	S L7 AND (CYCLIC GUANOSINE MONOPHOSPHATE (W) (PHOSPHODIESTERASE
L10	6	S L7 AND ("CGMP" OR "PDE5" OR "ANGIOTENSIN II RECEPTOR ANTAGONI

FILE 'REGISTRY' ENTERED AT 11:57:43 ON 02 MAR 2005

		E SILDENAFIL/CN
L11	2	S E3-E4
		E TADALAFIL/CN
L12	1	S E3
		E VARDENAFIL/CN
L13	3	S E3-E5
L14	1	S CANDESARTAN/CN

L15	2	E CANDESARTAN/CN S E3-E5
L16	2	E EPROSARTAN/CN S E3-E5
L17	4	E IRBESARTAN/CN S E3-E6
L18	4	E LOSARTAN/CN S E3-E7
L19	2	E OLMESARTAN/CN S E3-E5
L20	2	E SARALASIN/CN S E3-E4
L21	5	E TELMISARTAN/CN S E3-E7
L22	2	E VALSARTAN/CN S E3-E4
L23	6	S L11 OR L12 OR L13
L24	23	S L15 OR L16 OR L17 OR L18 OR L19 OR L20 OR L21 OR L22

FILE 'CAPLUS' ENTERED AT 12:02:01 ON 02 MAR 2005

L25	1081	S L23
L26	4320	S L24 E HYPERTENSION/BI
L27	78751	S E3, E16 E HYPERTENSION/CT
L28	43383	S E3

=> s l27 or l28

L29	78751	L27 OR L28
-----	-------	------------

=> s l29 or (high blood pressure) or (elevated blood pressure) or (increase? blood pressure)

3518588	HIGH
539	HIGHS
3518892	HIGH (HIGH OR HIGHS)
1174762	BLOOD
1191	BLOODS
1174891	BLOOD (BLOOD OR BLOODS)
1105830	PRESSURE
165382	PRESSURES
1168569	PRESSURE (PRESSURE OR PRESSURES)
1990	HIGH BLOOD PRESSURE (HIGH (W) BLOOD (W) PRESSURE)
240789	ELEVATED
1174762	BLOOD
1191	BLOODS
1174891	BLOOD (BLOOD OR BLOODS)
1105830	PRESSURE
165382	PRESSURES
1168569	PRESSURE (PRESSURE OR PRESSURES)
1047	ELEVATED BLOOD PRESSURE (ELEVATED (W) BLOOD (W) PRESSURE)
3402811	INCREASE?
1174762	BLOOD
1191	BLOODS
1174891	BLOOD (BLOOD OR BLOODS)
1105830	PRESSURE
165382	PRESSURES

1168569 PRESSURE

(PRESSURE OR PRESSURES)

2223 INCREASE? BLOOD PRESSURE

(INCREASE? (W) BLOOD (W) PRESSURE)

L30 80818 L29 OR (HIGH BLOOD PRESSURE) OR (ELEVATED BLOOD PRESSURE) OR
(INCREASE? BLOOD PRESSURE)

=> d his

(FILE 'HOME' ENTERED AT 11:49:08 ON 02 MAR 2005)

FILE 'CAPLUS' ENTERED AT 11:49:13 ON 02 MAR 2005

L1 E FOX DAVID/AU
69 S E2-E3, E20-E22
E HUGHES BERNADETTE/AU
L2 22 S E3-E4
E HUGHES B/AU
L3 40 S E3
E FOX D/AU
E FOX D?/AU
E FOX D/AU
L4 75 S E3
L5 144 S L1 OR L4
L6 62 S L2 OR L3
L7 204 S L5 OR L6
L8 10 S L7 AND HYPERTENSI?
L9 0 S L7 AND (CYCLIC GUANOSINE MONOPHOSPHATE (W) (PHOSPHODIESTERASE
L10 6 S L7 AND ("CGMP" OR "PDE5" OR "ANGIOTENSIN II RECEPTOR ANTAGONI

FILE 'REGISTRY' ENTERED AT 11:57:43 ON 02 MAR 2005

L11 E SILDENAFIL/CN
2 S E3-E4
E TADALAFIL/CN
L12 1 S E3
E VARDENAFIL/CN
L13 3 S E3-E5
L14 1 S CANDESARTAN/CN
E CANDESARTAN/CN
L15 2 S E3-E5
E EPROSARTAN/CN
L16 2 S E3-E5
E IRBESARTAN/CN
L17 4 S E3-E6
E LOSARTAN/CN
L18 4 S E3-E7
E OLMESARTAN/CN
L19 2 S E3-E5
E SARALASIN/CN
L20 2 S E3-E4
E TELMISARTAN/CN
L21 5 S E3-E7
E VALSARTAN/CN
L22 2 S E3-E4
L23 6 S L11 OR L12 OR L13
L24 23 S L15 OR L16 OR L17 OR L18 OR L19 OR L20 OR L21 OR L22

FILE 'CAPLUS' ENTERED AT 12:02:01 ON 02 MAR 2005

L25 1081 S L23
L26 4320 S L24
E HYPERTENSION/BI
L27 78751 S E3, E16
E HYPERTENSION/CT
L28 43383 S E3
L29 78751 S L27 OR L28

L30 80818 S L29 OR (HIGH BLOOD PRESSURE) OR (ELEVATED BLOOD PRESSURE) OR

=> s 125 and 126

L31 36 L25 AND L26

=> s 131 (L) 130

PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L31 (L) L30'

L32 9 L31 (L) L30

=> s 130 and 131

L33 9 L30 AND L31

=> d 133 1-9 ibib ed abs

L33 ANSWER 1 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2005:77981 CAPLUS

DOCUMENT NUMBER: 142:162662

TITLE: Nanoparticulate glipizide compositions

INVENTOR(S): Bosch, H. William; Ryde, Niels P.

PATENT ASSIGNEE(S): Elan Pharma International Limited, USA

SOURCE: U.S. Pat. Appl. Publ., 24 pp., Cont.-in-part of U.S.
Ser. No. 276,400.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 16

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005019412	A1	20050127	US 2003-701064	20031105
US 2002012675	A1	20020131	US 1999-337675	19990622
WO 2001087264	A2	20011122	WO 2001-US15983	20010518
WO 2001087264	A3	20020620		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT,
RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US,
UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

US 2004013613 A1 20040122 US 2003-276400 20030115

PRIORITY APPLN. INFO.: US 1998-164351 B2 19981001
US 1999-337675 A2 19990622
WO 2001-US15983 W 20010518
US 2003-276400 A2 20030115
US 2000-572961 A 20000518

ED Entered STN: 28 Jan 2005

AB The present invention is directed to nanoparticulate compns. comprising
glipizide. The glipizide particles of the composition preferably have an
effective average particle size of <2 μ . Thus, a formulation contained
spray-dried glipizide 5.33, mannitol 13.47, xylitol 40.53, citric acid
19.60, sodium bicarbonate 19.33, Asparatme 0.28, PEG-4000 0.93, and sodium
stearyl fumarate 0.53%.

L33 ANSWER 2 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:759835 CAPLUS

DOCUMENT NUMBER: 141:277616

TITLE: Preparation of 3-(1-[3-(1,3-benzothiazol-6-
yl)propylcarbamoyl]cycloalkyl)propanoic acid
derivatives as nep inhibitors

soluble secreted endopeptidase (SEP) of at least 1000 fold. These inhibitors have utility in a variety of therapeutic areas including the treatment of male and female sexual dysfunction, particularly female sexual dysfunction (FSD), especially wherein the FSD is female sexual arousal disorder (FSAD).

L33 ANSWER 3 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:546487 CAPLUS

DOCUMENT NUMBER: 141:106453

TITLE: Preparation of cyclopentyl glutaramide derivs. as neutral endopeptidase inhibitors

INVENTOR(S): . Dack, Kevin Neil; Owen, Dafydd Rhys; Watson, Christine Anne Louise

PATENT ASSIGNEE(S): Pfizer Limited, UK; Pfizer Inc.

SOURCE: PCT Int. Appl., 109 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004056787	A1	20040708	WO 2003-IB5981	20031212
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
US 2004138274	A1	20040715	US 2003-739426	20031218
NL 1025116	A1	20040624	NL 2003-1025116	20031223
NL 1025116	C2	20041018		

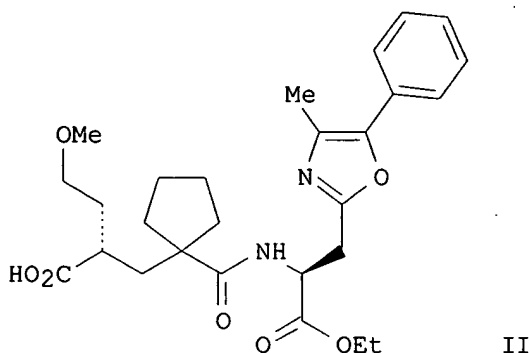
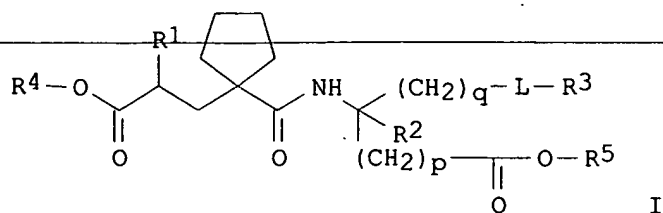
PRIORITY APPLN. INFO.:

GB 2002-30025 A 20021223
US 2003-448224P P 20030218

OTHER SOURCE(S): MARPAT 141:106453

ED Entered STN: 08 Jul 2004

GI



AB The title compds. I [R1 = C1-C6alkyl, C1-C6alkoxyC1-C3alkyl, or C1-C6alkoxyC1-C6alkoxyC1-C3alkyl; R2 = H or C1-C6alkyl; L = an aromatic heterocyclic ring, optionally substituted with C1-C6alkyl or halo; R3 = C1-C6alkyl optionally substituted by halo, alkoxy, haloalkoxy, alkylthio, haloalkylthio or nitrile group, or R3 is Ph or aromatic heterocyclyl each of which may be independently substituted by one or more alkyl, halo, haloalkyl, alkoxy, haloalkoxy, alkylthio, haloalkylthio or nitrile group; R4, R5 = either both hydrogen, or one of R4 and R5 is hydrogen and the other is a biolabile ester; p = 0-2; and q = 1 or 2] were prepared as neutral endopeptidase inhibitors for the treatment of cardiovascular disorders or related diseases. For example, reaction of (2S)-2-Amino-3-[5-(4-chlorophenyl)-oxazol-2-yl]-propionic acid Et ester hydrochloride (preparation given) and 1-[(2S)-2-(tert-butoxycarbonyl)-4-methoxybutyl]cyclopentanecarboxylic acid yielded (2S)-2-{1-[(1S)-1-Ethoxycarbonyl-2-(4-methyl-5-phenyl-oxazol-2-yl)-ethylcarbamoyl]-cyclopentylmethyl}-4-methoxy-butyric acid tert Bu ester, which when treated with trifluoroacetic acid furnished compound II. The prepared compds. are potent inhibitors of neutral endopeptidase.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L33 ANSWER 4 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:269863 CAPLUS

DOCUMENT NUMBER: 140:281417

TITLE: Combination therapy using antihypertensive agents and endothelin antagonists for vascular conditions associated with a male or female sexual dysfunction
INVENTOR(S): Adams, Michael A.; Hale, Taben M.; Heaton, Jeremy P. W.

PATENT ASSIGNEE(S): Queen's University At Kingston, Can.; Callegy Pharmaceuticals, Inc.

SOURCE: U.S. Pat. Appl. Publ., 29 pp., Cont.-in-part of U.S. Pat. Appl. 2003 8,020.

CODEN: USXXCO

DOCUMENT TYPE: Patent
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004063719	A1	20040401	US 2003-429197	20030502
US 6284763	B1	20010904	US 1999-382749	19990825
US 2002035067	A1	20020321	US 2001-902787	20010712
US 6458797	B2	20021001		
US 2003008020	A1	20030109	US 2002-192281	20020709
US 6787553	B2	20040907		
US 2004234619	A1	20041125	US 2004-869755	20040615
PRIORITY APPLN. INFO.:			US 1998-98178P	P 19980826
			US 1999-382749	A1 19990825
			US 2001-902787	A1 20010712
			US 2002-377917P	P 20020502
			US 2002-192281	A2 20020709

ED Entered STN: 02 Apr 2004

AB The present invention provides a method for a more efficacious treatment of a vascular condition through the administration of a therapeutically effective amount of a combination of an anti-pressor agent, an endothelin antagonist, and a sex hormone for repetitive cycles of on/off-treatment. In one embodiment, the invention provides a method for the prevention of tolerance induced by an anti-pressor agent via the inclusion of an endothelin antagonist in a combination therapy approach to remodel vascular structure and treat vascular conditions associated with a male or female sexual dysfunction, atherosclerosis, renal failure, **hypertension**, congestive heart failure, diabetic nephropathy, and diabetic neuropathy. The anti-pressor agent comprises one or more compds. such as prostaglandin-E 1, an ACE inhibitor, an angiotensin-II receptor antagonist, an α 1-adrenergic receptor antagonist, a β -adrenergic receptor antagonist, a calcium channel blocker, an activator of guanylyl cyclase or adenylyl cyclase, a phosphodiesterase inhibitor, and hydralazine. The endothelin antagonist comprises one or more compds. such as a peptidal endothelin antagonist, a non-peptidal endothelin antagonist, and an inhibitor of endothelin converting enzyme. Such a combination therapy approach enhances the efficacy of the anti-pressor agent and enables an increase in the frequency and duration of anti-pressor administrations for the long term treatment of vascular conditions.

L33 ANSWER 5 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:60341 CAPLUS

DOCUMENT NUMBER: 140:117406

TITLE: Liquid dosage compositions of stable nanoparticulate drugs

INVENTOR(S): Bosch, William H.; Hilborn, Matthew R.; Hovey, Douglas C.; Kline, Laura J.; Lee, Robert W.; Pruitt, John D.; Ryde, Niels P.; Ryde, Tuula A.; Xu, Shuqian

PATENT ASSIGNEE(S): Elan Pharma International, Ltd, Ire.

SOURCE: PCT Int. Appl., 68 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 16

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004006959	A1	20040122	WO 2003-US22187	20030716
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN,			

TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
 RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
 KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
 FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,
 BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2002-396530P P 20020716

ED Entered STN: 26 Jan 2004

AB The present invention relates to liquid dosage compns. of stable nanoparticulate drugs. The liquid dosage compns. of the invention include osmotically active crystal growth inhibitors that stabilize the nanoparticulate active agents against crystal and particle size growth of the drug. Thus, an aqueous nanoparticulate colloidal dispersion (NCD) comprising drug 32.5 Copovidone 6.5, and dioctyl sodium sulfosuccinate 0.464% by weight was prepared by milling for 3.8 h under high energy milling conditions. The final mean particle size (by weight) of the drug particles was 161 nm. The concentrated NCD was then diluted with preserved water and glycerol (the osmotically active crystal growth inhibitor) to 0.5-3.0% drug.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L33 ANSWER 6 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:20474 CAPLUS

DOCUMENT NUMBER: 140:71026

TITLE: Novel combination for treating **hypertension**

INVENTOR(S): Fox, David Nathan Abraham; Hughes, Bernadette

PATENT ASSIGNEE(S): Pfizer, Limited, UK; Pfizer, Inc.

SOURCE: PCT Int. Appl., 25 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004002461	A2	20040108	WO 2003-IB2657	20030616
WO 2004002461	A3	20040513		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
US 2004132731	A1	20040708	US 2003-603369	20030625
PRIORITY APPLN. INFO.:			GB 2002-14784	A 20020626
			US 2002-396780P	P 20020717

ED Entered STN: 11 Jan 2004

AB Combinations comprising a) an inhibitor of cyclic guanosine monophosphate (cGMP) specific phosphodiesterase type 5 (PDE5) and b) an angiotensin II receptor antagonist are useful for treating **hypertension**. In the example provided the combined effect in **hypertensive** rats of candesartan and a PDE5 inhibitor was significantly larger than the sum of the 2 individual effects.

L33 ANSWER 7 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2003:396889 CAPLUS

DOCUMENT NUMBER: 138:401744

TITLE: Preparation of polycyclic guanine derivative phosphodiesterase V inhibitors

INVENTOR(S): Asberom, Theodros; Clader, John W.; Hu, Yueqing;
Pissarnitski, Dmitri A.; Stamford, Andrew W.; Xu, Ruo

PATENT ASSIGNEE(S): Schering Corporation, USA
SOURCE: PCT Int. Appl., 95 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003042216	A1	20030522	WO 2002-US35721	20021107
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LU, LV, MA, MD, MG, MK, MN, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SC, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UZ, VC, VN, YU, ZA, ZM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2003176413	A1	20030918	US 2002-290011	20021107
EP 1442042	A1	20040804	EP 2002-786685	20021107
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
PRIORITY APPLN. INFO.:			US 2001-344498P	P 20011109
			WO 2002-US35721	W 20021107
OTHER SOURCE(S): MARPAT 138:401744				
ED Entered STN: 23 May 2003				
GI				

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. I [q = 0-2; R1, R3-6 = H, alkyl, aryl, heteroaryl, cycloalkyl, heterocycloalkyl; R2 = H, halo, alkyl, alkoxy, etc.; Y = alkyl, aryl] are prepared For instance, 4-amino-1-benzyl-5-(ethoxycarbonyl)imidazole (preparation given) is treated with ethylisocyanate (o-xylene, reflux, 16 h), the resulting product cyclized (MeOH, NaOMe, reflux, 4 h), subsequently treated with POCl3 and the product used to alkylate (R)-2-amino-3-phenylpropanol (NMP, 130°, 12 h) which provides II. II is treated with MsCl (Et3N), debenzylated (MeOH, NH4O2CH, Pd(OH)2/C, reflux, 3 h), brominated (HOAc, NaOAc, Br2), alkylated with 3-chloro-4-methoxybenzyl bromide (DMF, K2CO3) and treated with NaOEt (DMF/EtOH) to afford III. III has IC50 < 4.1 nM for PDE V and IC50 > 300 nM for PDE VI. I are useful for treating sexual dysfunction.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L33 ANSWER 8 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2001:338762 CAPLUS
DOCUMENT NUMBER: 134:362292
TITLE: Methods of determining individual hypersensitivity to a pharmaceutical agent from gene expression profile
INVENTOR(S): Farr, Spencer
PATENT ASSIGNEE(S): Phase-1 Molecular Toxicology, USA
SOURCE: PCT Int. Appl., 222 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001032928	A2	20010510	WO 2000-US30474	20001103
WO 2001032928	A3	20020725		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
PRIORITY APPLN. INFO.:			US 1999-165398P	P 19991105
			US 2000-196571P	P 20000411
ED Entered STN: 11 May 2001				
AB The invention discloses methods, gene databases, gene arrays, protein arrays, and devices that may be used to determine the hypersensitivity of individuals to a given agent, such as drug or other chemical, in order to prevent toxic side effects. In one embodiment, methods of identifying hypersensitivity in a subject by obtaining a gene expression profile of multiple genes associated with hypersensitivity of the subject suspected to be hypersensitive, and identifying in the gene expression profile of the subject a pattern of gene expression of the genes associated with hypersensitivity are disclosed. The gene expression profile of the subject may be compared with the gene expression profile of a normal individual and a hypersensitive individual. The gene expression profile of the subject that is obtained may comprise a profile of levels of mRNA or cDNA. The gene expression profile may be obtained by using an array of nucleic acid probes for the plurality of genes associated with hypersensitivity. The expression of the genes predetd. to be associated with hypersensitivity is directly related to prevention or repair of toxic damage at the tissue, organ or system level. Gene databases arrays and apparatus useful for identifying hypersensitivity in a subject are also disclosed.				
L33 ANSWER 9 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN				
ACCESSION NUMBER:		2000:161149 CAPLUS		
DOCUMENT NUMBER:		132:203141		
TITLE:		Anti-pressor agents and methods for remodeling neuronal and cardiovascular pathways for the long term management of sexual dysfunction		
INVENTOR(S):		Adams, Michael A.; Heaton, Jeremy P. W.		
PATENT ASSIGNEE(S):		Queen's University At Kingston, Can.		
SOURCE:		PCT Int. Appl., 37 pp.		
		CODEN: PIXXD2		
DOCUMENT TYPE:		Patent		
LANGUAGE:		English		
FAMILY ACC. NUM. COUNT:		2		
PATENT INFORMATION:				

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000012110	A2	20000309	WO 1999-CA787	19990825
WO 2000012110	A3	20000803		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK,				

ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG,
CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

CA 2340206	AA	20000309	CA 1999-2340206	19990825
AU 9954034	A1	20000321	AU 1999-54034	19990825
EP 1235563	A2	20020904	EP 1999-939874	19990825

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, LT, LV, FI, RO, MK, CY, AL

PRIORITY APPLN. INFO.:	US 1998-98178P	P 19980826
	WO 1999-CA787	W 19990825

ED Entered STN: 10 Mar 2000

AB The invention provides a method of administration of an agent which acts to remodel neuronal or vascular pathways for the long term management of sexual dysfunction in both males and females. In a preferred embodiment, the invention provides a method of ameliorating or reversing pathogenic vascular degradative modeling in the ilio-hypogastric-pudendal arterial bed and genitalia comprising administering to a human patient in need of such treatment a therapeutically effective amount of an anti-pressor agent. The anti-pressor agent comprises one or more compds. selected from the therapeutic classes of direct vasodilators such as hydralazine and NO donors, ACE inhibitors, angiotensin-II receptor antagonists, α 1-adrenergic receptor antagonists, β -adrenergic receptor antagonists, calcium channel blockers, and phosphodiesterase inhibitors. The anti-pressor agent may be co-administered with a diuretic compound, and is administered either chronically at low dose, or for short periods of time at doses higher than are typically used for the treatment of **hypertension**. In certain embodiments of the method of the invention, the anti-pressor agent is co-administered with a diuretic agent and/or prostaglandin-E1.

=> d his

(FILE 'HOME' ENTERED AT 11:49:08 ON 02 MAR 2005)

FILE 'CAPLUS' ENTERED AT 11:49:13 ON 02 MAR 2005

	E FOX DAVID/AU
L1	69 S E2-E3, E20-E22
	E HUGHES BERNADETTE/AU
L2	22 S E3-E4
	E HUGHES B/AU
L3	40 S E3
	E FOX D/AU
	E FOX D?/AU
	E FOX D/AU
L4	75 S E3
L5	144 S L1 OR L4
L6	62 S L2 OR L3
L7	204 S L5 OR L6
L8	10 S L7 AND HYPERTENSI?
L9	0 S L7 AND (CYCLIC GUANOSINE MONOPHOSPHATE (W) (PHOSPHODIESTERASE
L10	6 S L7 AND ("CGMP" OR "PDE5" OR "ANGIOTENSIN II RECEPTOR ANTAGONI

FILE 'REGISTRY' ENTERED AT 11:57:43 ON 02 MAR 2005

	E SILDENAFIL/CN
L11	2 S E3-E4
	E TADALAFIL/CN
L12	1 S E3
	E VARDENAFIL/CN
L13	3 S E3-E5
L14	1 S CANDESARTAN/CN
	E CANDESARTAN/CN
L15	2 S E3-E5
	E EPROSARTAN/CN
L16	2 S E3-E5

L17	4	E IRBESARTAN/CN S E3-E6
L18	4	E LOSARTAN/CN S E3-E7
L19	2	E OLMESARTAN/CN S E3-E5
L20	2	E SARALASIN/CN S E3-E4
L21	5	E TELMISARTAN/CN S E3-E7
L22	2	E VALSARTAN/CN S E3-E4
L23	6	S L11 OR L12 OR L13
L24	23	S L15 OR L16 OR L17 OR L18 OR L19 OR L20 OR L21 OR L22

FILE 'CAPLUS' ENTERED AT 12:02:01 ON 02 MAR 2005

L25	1081	S L23
L26	4320	S L24 E HYPERTENSION/BI
L27	78751	S E3, E16 E HYPERTENSION/CT
L28	43383	S E3
L29	78751	S L27 OR L28
L30	80818	S L29 OR (HIGH BLOOD PRESSURE) OR (ELEVATED BLOOD PRESSURE) OR
L31	36	S L25 AND L26
L32	9	S L31 (L) L30
L33	9	S L30 AND L31

=> s 125 (L) 130
L34 34 L25 (L) L30

=> s 126 (L) 130
L35 1025 L26 (L) L30

=> s 134 and 135
L36 0 L34 AND L35

=> s 131 and hypertens?
79500 HYPERTENS?
L37 9 L31 AND HYPERTENS?

=> s 137 not 133
L38 0 L37 NOT L33

=> s "CGMP" or "PDE5" or (cyclic guanosine monophosphate (w) phosphodiesterase)

20057	"CGMP"
187	"CGMPS"
20081	"CGMP"
	("CGMP" OR "CGMPS")
533	"PDE5"
286246	CYCLIC
330	CYCLICS
286374	CYCLIC
	(CYCLIC OR CYCLICS)
21456	GUANOSINE
313	GUANOSINES
21565	GUANOSINE
	(GUANOSINE OR GUANOSINES)
29181	MONOPHOSPHATE
3848	MONOPHOSPHATES
31896	MONOPHOSPHATE
	(MONOPHOSPHATE OR MONOPHOSPHATES)
835	CYCLIC GUANOSINE MONOPHOSPHATE
	(CYCLIC (W) GUANOSINE (W) MONOPHOSPHATE)

24057 PHOSPHODIESTERASE
 2560 PHOSPHODIESTERASES
 24563 PHOSPHODIESTERASE
 (PHOSPHODIESTERASE OR PHOSPHODIESTERASES)
 33 CYCLIC GUANOSINE MONOPHOSPHATE (W) PHOSPHODIESTERASE
 L39 20335 "CGMP" OR "PDE5" OR (CYCLIC GUANOSINE MONOPHOSPHATE (W) PHOSPHODIESTERASE)

=> s (angiotensin (L) receptor antagonist) or (angiotensin receptor antagonist) or "angiotensin II receptor antagonist"

54762 ANGIOTENSIN
 1691 ANGIOTENSINS
 54850 ANGIOTENSIN
 (ANGIOTENSIN OR ANGIOTENSINS)
 591069 RECEPTOR
 542204 RECEPTORS
 703691 RECEPTOR
 (RECEPTOR OR RECEPTORS)
 149224 ANTAGONIST
 108335 ANTAGONISTS
 200876 ANTAGONIST
 (ANTAGONIST OR ANTAGONISTS)
 66210 RECEPTOR ANTAGONIST
 (RECEPTOR(W)ANTAGONIST)
 6539 ANGIOTENSIN (L) RECEPTOR ANTAGONIST
 54762 ANGIOTENSIN
 1691 ANGIOTENSINS
 54850 ANGIOTENSIN
 (ANGIOTENSIN OR ANGIOTENSINS)
 591069 RECEPTOR
 542204 RECEPTORS
 703691 RECEPTOR
 (RECEPTOR OR RECEPTORS)
 149224 ANTAGONIST
 108335 ANTAGONISTS
 200876 ANTAGONIST
 (ANTAGONIST OR ANTAGONISTS)
 2785 ANGIOTENSIN RECEPTOR ANTAGONIST
 (ANGIOTENSIN(W)RECEPTOR(W)ANTAGONIST)
 54762 "ANGIOTENSIN"
 1691 "ANGIOTENSINS"
 54850 "ANGIOTENSIN"
 ("ANGIOTENSIN" OR "ANGIOTENSINS")
 2015064 "II"
 825 "IIS"
 2015534 "II"
 ("II" OR "IIS")
 591069 "RECEPTOR"
 542204 "RECEPTORS"
 703691 "RECEPTOR"
 ("RECEPTOR" OR "RECEPTORS")
 149224 "ANTAGONIST"
 108335 "ANTAGONISTS"
 200876 "ANTAGONIST"
 ("ANTAGONIST" OR "ANTAGONISTS")
 1675 "ANGIOTENSIN II RECEPTOR ANTAGONIST"
 ("ANGIOTENSIN"(W)"II"(W)"RECEPTOR"(W)"ANTAGONIST")

L40 6539 (ANGIOTENSIN (L) RECEPTOR ANTAGONIST) OR (ANGIOTENSIN RECEPTOR ANTAGONIST) OR "ANGIOTENSIN II RECEPTOR ANTAGONIST"

=> s 139 (L) 140

L41 80 L39 (L) L40

=> s 141 and hypertens?

79500 HYPERTENS?

L42 17 L41 AND HYPERTENS?

=> s 142 not 133

L43 16 L42 NOT L33

=> d 143 1-16 ibib ed abs

L43 ANSWER 1 OF 16 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:965255 CAPLUS

DOCUMENT NUMBER: 141:410950

TITLE: Preparation of 5,7-diaminopyrazolo[4,3-d]pyrimidines as selective PDE5 inhibitors useful in the treatment of **hypertension**

INVENTOR(S): Bell, Andrew Simon; Brown, David Graham; Fox, David Nathan Abraham; Marsh, Ian Roger; Morrell, Andrew Ian; Palmer, Michael John; Winslow, Carol Ann

PATENT ASSIGNEE(S): Pfizer Limited, UK; Pfizer Inc.

SOURCE: PCT Int. Appl., 279 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004096810	A1	20041111	WO 2004-IB1433	20040422
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
NL 1026074	A1	20041101	NL 2004-1026074	20040428
US 2005043325	A1	20050224	US 2004-834484	20040429
PRIORITY APPLN. INFO.:			GB 2003-9780	A 20030429
			GB 2003-27748	A 20031128
			US 2003-476678P	P 20030606
			US 2004-538147P	P 20040120

OTHER SOURCE(S): MARPAT 141:410950

ED Entered STN: 12 Nov 2004

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. I [wherein R1 = (un)substituted cycloalkyl, cycloalkenyl, (un)substituted pyridin-2-yl, (un)fused Ph, etc.; R2 = H, alkyl; R3, R4 = independently (un)substituted alkyl, alkenyl, cycloalkyl, etc.; or NR3R4 = piperazin-1-yl, monocyclic, saturated polycyclic; R5 = (un)substituted halo/alkyl, alkenyl, alkynyl, cycloalkyl; R6 = H, (un)substituted alkyl, haloalkyl, alkenyl, alkynyl, etc.] were prepared as selective PDE5 inhibitors. For example, II•2HCl was prepared from (4-Methylpyridin-2-yl)amine, dichloride III (general preparation given), and tert-Bu piperazine-1-carboxylate. I gave IC50 values < 10,000 nM in an in vitro assay for PDE5 inhibition. Thus, I are used for treating

hypertension.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L43 ANSWER 2 OF 16 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:884340 CAPLUS

DOCUMENT NUMBER: 141:389246

TITLE: Angiotensin-(1-7) Inhibitory Mechanism of
Norepinephrine Release in **Hypertensive** Rats

AUTHOR(S): Gironacci, Mariela M.; Valera, Maria S.; Yujnovsky,
Irene; Pena, Clara

CORPORATE SOURCE: Departamento de Quimica Biologica, Instituto de
Quimica y Fisicoquimica Biologicas, Facultad de
Farmacia y Bioquimica, Universidad de Buenos Aires,
Argent.

SOURCE: Hypertension (2004), 44(5), 783-787

CODEN: HPRTDN; ISSN: 0194-911X

PUBLISHER: Lippincott Williams & Wilkins

DOCUMENT TYPE: Journal

LANGUAGE: English

ED Entered STN: 25 Oct 2004

AB Release of norepinephrine (NE) by the hypothalamic nuclei may contribute
to regulation of sympathetic nervous system (SNS) activity.

Angiotensin-(1-7) [Ang-(1-7)] has an antihypertensive effect and
may decrease SNS activity. We tested the hypothesis that Ang-(1-7)
inhibits the release of NE in hypothalami, via the Ang-(1-7) and
angiotensin II type 2 (AT2) receptors, acting through a bradykinin
(BK)/NO-dependent mechanism. Hypothalami from normotensive controls and
spontaneously **hypertensive** rats (SHR) were isolated and
endogenous NE stores labeled by incubating the tissues with [3H]NE.
[3H]NE release from the hypothalami was stimulated by KCl in the presence
or absence of Ang-(1-7) alone or combined with various antagonists and
inhibitors. Ang-(1-7) significantly attenuated K+-induced NE release by
hypothalami from normotensive rats but was more potent in SHR. The
Ang-(1-7) **receptor antagonist** [D-Ala7]Ang-(1-7), the
AT2 **receptor antagonist** PD 123319, and the BK B2
receptor antagonist icatibant all blocked the inhibitory
effect of Ang-(1-7) on K+-stimulated NE release in SHR. The inhibitory
effect of Ang-(1-7) disappeared in the presence of the NO synthase
inhibitor NG-nitro-L-arginine Me ester and was restored by the precursor
of NO, L-arginine. The diminished NE release caused by Ang-(1-7) was
blocked by a soluble guanylyl cyclase inhibitor as well as by a **cGMP**
-dependent protein kinase (PKG). We concluded that Ang-(1-7) decreases NE
release from the hypothalamus via the Ang-(1-7) or AT2 receptors, acting
through a BK/NO-mediated mechanism that stimulates **cGMP**/PKG
signaling. In this way, Ang-(1-7) may decrease SNS activity and exert an
antihypertensive effect.

REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L43 ANSWER 3 OF 16 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:544960 CAPLUS

DOCUMENT NUMBER: 141:188914

TITLE: RhoA activation in vascular smooth muscle cells from
stroke-prone spontaneously **hypertensive** rats

AUTHOR(S): Moriki, Nobuyuki; Ito, Masaaki; Seko, Tetsuya;
Kureishi, Yasuko; Okamoto, Ryuji; Nakakuki, Tetsuya;
Kongo, Mariko; Isaka, Naoki; Kaibuchi, Kozo; Nakano,
Takeshi

CORPORATE SOURCE: First Department of Internal Medicine, Mie University
School of Medicine, Tsu, Japan

SOURCE: Hypertension Research (2004), 27(4), 263-270

CODEN: HRESE4; ISSN: 0916-9636

PUBLISHER: Japanese Society of Hypertension

DOCUMENT TYPE: Journal
LANGUAGE: English

ED Entered STN: 08 Jul 2004

AB RhoA is commonly activated in the aorta in various **hypertensive** models, indicating that RhoA seems to be a mol. switch in **hypertension**. The mol. mechanisms for RhoA activation in stroke-prone spontaneously **hypertensive** rats (SHRSP) were here investigated using cultured aortic smooth muscle cells (VSMC). The level of the active form of RhoA was higher in VSMC from SHRSP than in those from Wistar-Kyoto rats (WKY). The phosphorylation level of myosin phosphatase target subunit 1 (MYPT1) at the inhibitory site was also significantly higher in SHRSP, and the phosphorylation levels in both VSMCs were strongly inhibited to a similar extent by treatment with Y-27632, a Rho-kinase inhibitor. The expression levels of RhoA/Rho-kinase related mols., namely RhoA, Rho-kinase, MYPT1, CPI-17 (inhibitory phosphoprotein for myosin phosphatase) and myosin light chain kinase, were not different between SHRSP and WKY. Valsartan, an **angiotensin** II (Ang II)-type 1 **receptor antagonist**, selectively and significantly reduced the RhoA activation in VSMC from SHRSP. The expression levels of the Rho GDP-dissociation inhibitor (RhoGDI) and leukemia-associated Rho-specific guanine nucleotide exchange factor (RhoGEF) did not differ between SHRSP and WKY. In cyclic nucleotide signaling, cyclic GMP (**cGMP**)-dependent protein kinase I α (cGKI α) was significantly downregulated in SHRSP cells, although there were no changes in the expression levels of guanylate cyclase β and cAMP-dependent protein kinase or the intracellular contents of **cGMP** and cAMP between the two rat models. These results suggest that the possible mechanisms underlying RhoA activation in VSMC from SHRSP are autocrine/paracrine regulation by Ang II and/or cGKI α downregulation.

L43 ANSWER 4 OF 16 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:296093 CAPLUS

DOCUMENT NUMBER: 141:307251

TITLE: Effect of angiotensin II type 1 (at1) receptor antagonist on the endothelial dysfunction in spontaneously **hypertensive** rats in correlation with the nitric oxide system

AUTHOR(S): Slaninka-Miceska, M.; Bogdanska, J.; Korneti, P.; Kostova, E.; Jovanoska, E.; Petrov, S.

CORPORATE SOURCE: Medical Faculty, Department of Preclinical and Clinical Pharmacology and Toxicology, Skopje, Macedonia

SOURCE: Bratislavske Lekarske Listy (2003), 104(11), 342-346
CODEN: BLLIAX; ISSN: 0006-9248

PUBLISHER: Slovak Academic Press Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

ED Entered STN: 12 Apr 2004

AB Background: **Hypertension** is associated with impaired endothelial function, which can be explained by a decrease in nitric oxide (NO) generation or by an enhanced inactivation of NO after its release from endothelial cells. Objectives: The aim of this study was to investigate the effect of long-term treatment with losartan, an **angiotensin** II (AT1) **receptor antagonist**, on endothelial dysfunction in an animal model of **hypertension** in relation to the nitric oxide system. Methods: Losartan was administered to 48 sixteen-week-old spontaneously **hypertensive** rats, in a dose of 10 mg/kg bw/daily in drinking water, for 12 wk. Systolic blood pressure (SBP) was measured at the beginning, after 4, 8 and 12 wk of treatment, by the tail-cuff plethysmograph method. At each mentioned time point, a group of 12 animals was sacrificed and blood was withdrawn from the abdominal aorta. Plasma samples were used for determination of total nitrate/nitrite levels, cyclic guanosine monophosphate (**cGMP**) and endothelin

(ET) 1 levels. Statistical evaluation of the results was performed by the use of a computer statistical program Statistica for Windows 5.0.

Results: Losartan produced a significant decrease of SBP at all time points. On the other hand, long-term treatment with this AT1 **receptor antagonist** produced a significant increase of nitrate/nitrite and **cGMP** plasma levels. When we compared the values of SBP with plasma nitrate/nitrite as well as with **cGMP** values, a statistically significant correlation was established. A statistically significant decrease in plasma endothelin 1 values was found during the whole study period. Also, a pos. correlation between SBP and plasma endothelin 1 concns. was observed. Conclusions: Long-term losartan (AT1 **receptor antagonist**) treatment, apart from its blood pressure lowering effect in **hypertension**, has beneficial effects on the endothelial dysfunction which is at least partially due to the activation of the nitric oxide system.

REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L43 ANSWER 5 OF 16 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2003:273646 CAPLUS

DOCUMENT NUMBER: 139:177918

TITLE: The vascular response to the K⁺ channel inhibitor 4-aminopyridine in **hypertensive** rats

AUTHOR(S): Berg, Torill

CORPORATE SOURCE: Institute for Basic Medical Sciences, Department of Physiology, University of Oslo, Oslo, 0317, Norway
SOURCE: European Journal of Pharmacology (2003), 466(3), 301-310

CODEN: EJPHAZ; ISSN: 0014-2999

PUBLISHER: Elsevier Science B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

ED Entered STN: 09 Apr 2003

AB The K⁺ channel inhibitor 4-aminopyridine induced an immediate increase in blood pressure and tension in spontaneously **hypertensive** rats (SHR). Further anal. strongly suggested this to be due to closure of vascular smooth muscle K⁺ channels, as previously concluded for normotensive rats (WKY). The tension response was greater in SHR than WKY, suggesting an increased channel activity to compensate for the high total peripheral vascular resistance in SHR. The response was enhanced after nitric oxide (NO) synthase inhibitor in both strains, probably reflecting increased channel activity after elimination of the NO-**cGMP** pathway. The response in SHR but not WKY was increased after α 1-adrenoceptor inhibition and adrenalectomy but not sympathetic nerve transmitter depletion. It increased also after **angiotensin** AT1 and endothelin ETA **receptor antagonists** and protein kinase C inhibitor. These results indicated an increased adrenal catecholamine, **angiotensin** AT1 and endothelin ETA activation of the phospholipase C-protein kinase C pathway in SHR, inhibiting the 4-aminopyridine-sensitive K⁺ channels.

REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L43 ANSWER 6 OF 16 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2002:526570 CAPLUS

DOCUMENT NUMBER: 138:100636

TITLE: Dual ACE and NEP inhibitor MDL-100,240 prevents and regresses severe angiotensin II-dependent **hypertension** partially through bradykinin type 2 receptor

AUTHOR(S): Rossi, Gian Paolo; Cavallin, Martina; Rizzoni, Damiano; Bova, Sergio; Mazzocchi, Giuseppina; Agabiti-Rosei, Enrico; Nussdorfer, Gastone G.; Pessina, Achille C.

CORPORATE SOURCE: Department of Medical and Surgical Sciences,
University of Brescia, Brescia, Italy

SOURCE: Journal of Hypertension (2002), 20(7), 1451-1459
CODEN: JOHYD3; ISSN: 0263-6352

PUBLISHER: Lippincott Williams & Wilkins

DOCUMENT TYPE: Journal

LANGUAGE: English

ED Entered STN: 16 Jul 2002

AB To investigate the effects of the dual **angiotensin**-converting enzyme (ACE) + neutral endopeptidase (NEP) inhibitor, MDL-100,240 (MDL), on **hypertension** and cardiovascular damage in male heterozygous transgenic Ren2 rats. Blood-pressure-matched 5-wk-old transgenic rats were allocated to receive a placebo, MDL (40 mg/kg body weight) or ramipril (5 mg/kg body weight) for 8 wk. During the last 4 wk, the bradykinin B2 **receptor antagonist**, icatibant (0.5 mg/kg body weight), was also administered s.c. via osmotic minipumps to 50% of the transgenic rats receiving MDL or ramipril. We measured blood pressure, heart weight, structural changes in the aorta and small resistance mesenteric arteries, and the plasma concns. of adrenomedullin, aldosterone, atrial natriuretic peptide and **cGMP**. To verify if MDL could regress long-standing **hypertension** and full-blown cardiovascular damage, 3-mo-old transgenic rats received MDL s.c. (3 and 10 mg/kg body weight, osmotic minipumps) for 4 wk. Compared with placebo, MDL decreased blood pressure ($P < 0.001$) and prevented left ventricular hypertrophy ($P < 0.001$), being as effective as ramipril. Hypertrophy and dilatation of the aorta and hypertrophy of the resistance arterioles were all prevented by MDL. Plasma aldosterone was decreased by MDL ($P < 0.001$), but not by ramipril. Icatibant blunted the decrease in blood pressure ($P < 0.001$), decreased **cGMP** concns. and blunted the decrease in cross-sectional area of the resistance arteries in MDL-treated, but not in ramipril-treated, transgenic rats. In 3-mo-old transgenic rats, MDL normalized blood pressure, regressed left ventricular hypertrophy and decreased adrenomedullin concns. The dual ACE+NEP inhibitor MDL prevented and regressed severe **hypertension** and cardiovascular damage, even in this model of severe **angiotensin** II-dependent **hypertension** with pronounced cardiovascular damage. Enhancement of the effects of bradykinin has a role in such favorable outcomes.

REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L43 ANSWER 7 OF 16 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2002:469978 CAPLUS

DOCUMENT NUMBER: 137:367891

TITLE: Renoprotective Mechanisms of Angiotensin II Antagonism in Experimental Chronic Renal Failure

AUTHOR(S): Uhlenius, Nina; Miettinen, Aaro; Vuolteenaho, Olli; Tikkanen, Ilkka

CORPORATE SOURCE: Haartman Institute, Minerva Foundation Institute for Medical Research, University of Helsinki, Helsinki, Finland

SOURCE: Kidney & Blood Pressure Research (2002), 25(2), 71-79
CODEN: KBPRFC; ISSN: 1420-4096

PUBLISHER: S. Karger AG

DOCUMENT TYPE: Journal

LANGUAGE: English

ED Entered STN: 24 Jun 2002

AB Aims: We investigated **angiotensin** II and nitric oxide-**cGMP** pathway in the development of **hypertension** and renal damage in chronic exptl. nephritis. Methods: Rats with autoimmune nephritis were treated for 12 wk with AT1 **receptor antagonist** L-158,809 and/or ACE inhibitor captopril given in drinking water. Blood pressure, urinary albumin, and urinary excretion of **cGMP** were measured. Renal d. of ACE, AT1 and AT2 receptors was determined by quant. in vitro autoradiog. Results: L-158,809, captopril, and

their combination decreased blood pressure and normalized urinary albumin excretion rate in rats with nephritis. In L-158,809-treated rats, **cGMP** excretion was increased compared to the vehicle-treated nephritic group suggesting that the dysfunctional nitric oxide system may be activated by **angiotensin** antagonism. In nephritic rats, AT1 and AT2 receptor binding densities in renal medulla were decreased, cortical AT receptor expression remained unchanged. Following L-158,809 treatment, both AT1 and AT2 receptor binding was suppressed. Conclusion: Long-term blockade of AT1 receptors in chronic nephritis has beneficial effects both on albuminuria and blood pressure being as effective as ACE inhibition or their combination. The stimulatory effect of AT1 receptor antagonism on **cGMP** production was not mediated by AT2 receptor-dependent mechanisms suggesting that AT1 receptor blockade per se favors activation of humoral pathways that stimulate **cGMP** production and potentially contribute to renal protection in chronic nephritis.

REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L43 ANSWER 8 OF 16 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2002:145890 CAPLUS

DOCUMENT NUMBER: 137:195283

TITLE: Renin-angiotensin blockade improves renal **cGMP** production via non-AT2-receptor mediated mechanisms in **hypertension**-induced by chronic NOS inhibition in rat

AUTHOR(S): Uhlenius, Nina; Vuolteenaho, Olli; Tikkanen, Ilkka

CORPORATE SOURCE: Institute for Medical Research, Minerva Foundation, Helsinki, FIN-00250, Finland

SOURCE: JRAAS (2001), 2(4), 233-239

CODEN: JRAAAG; ISSN: 1470-3203

PUBLISHER: JRAAS Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

ED Entered STN: 26 Feb 2002

AB Background To investigate the changes in the **angiotensin** II (Ang II) receptors and nitric oxide (NO)-**cGMP** pathway in the rat kidney after nitric oxide synthase (NOS) blockade. Methods Captopril, an **angiotensin**-converting enzyme (ACE) inhibitor, 20 mg/100 mL; and/or L-158,809 (an Ang II AT1-receptor antagonist, 5 mg/100 mL) and L-NAME (NOS inhibitor, 50 mg/100 mL) were administered orally for 12 wk. Blood pressure (BP), urinary albumin, urinary **cGMP** excretion, plasma ANP, and plasma renin activity were measured. In vitro autoradiog. was used to locate the Ang II receptors in the kidney. Results Captopril and L-158,809 treatments normalized BP and prevented the appearance of albuminuria in rats receiving L-NAME. Urinary **cGMP** excretion was significantly increased in L-158,809-treated rats compared with the non-treated group, suggesting that the dysfunctional NO system may be activated by the treatment. AT1-receptor binding in the kidney was inhibited to about 40% of the control value after administration of L-158,809. The AT2-receptor binding was inhibited to less than 15% of the control value. NOS inhibition had no effect on receptor binding. Conclusion Blockade of NOS causes **hypertension** and renal damage. Treatment with an ACE inhibitor and/or Ang II **receptor antagonist** prevented these changes equally effectively. The stimulatory effect of AT1-receptor antagonism on **cGMP** production was not mediated by AT2-receptor-dependent mechanisms, since renal AT2-receptor binding d. was suppressed following treatment with L-158,809. AT1-receptor blockade per se favors activation of humoral pathways that stimulate **cGMP** production potentially contributing to renal and vascular protection in **hypertension** and chronic renal disease.

REFERENCE COUNT: 51 THERE ARE 51 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L43 ANSWER 9 OF 16 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2001:614955 CAPLUS

DOCUMENT NUMBER: 135:366494

TITLE: Angiotensin-converting enzyme inhibition potentiates angiotensin II type 1 receptor effects on renal bradykinin and cGMP

AUTHOR(S): Siragy, Helmy M.; De Gasparo, Marc; El-Kersh, Mohamed; Carey, Robert M.

CORPORATE SOURCE: Department of Medicine, University of Virginia Health Sciences Center, Charlottesville, VA, 22908, USA

SOURCE: Hypertension (2001), 38(2), 183-186

CODEN: HPRTDN; ISSN: 0194-911X

PUBLISHER: Lippincott Williams & Wilkins

DOCUMENT TYPE: Journal

LANGUAGE: English

ED Entered STN: 24 Aug 2001

AB Angiotensin (Ang) receptor blockers (ARBs) increase bradykinin (BK) by antagonizing Ang II at its type I (AT1) receptors and diverting Ang II to its counterregulatory type 2 (AT2) receptors. Because the effect of ARBs on BK is constrained by the short half-life of BK and because ACE inhibitors block the degradation of BK, this study was designed to test the hypothesis that an ACE inhibitor can potentiate ARB-induced increases in renal interstitial fluid (RIF) BK levels. The authors used a microdialysis technique to recover BK and cGMP in vivo from the RIF of sodium-depleted, conscious Sprague-Dawley rats infused for 60 min with the AT2 receptor blocker valsartan (0.17 mg/kg per min), with the active metabolite of the ACE inhibitor benazepril (benazeprilat. 0.05 mg/kg per min), or with the specific AT2 receptor blocker PD 123,319 (50 µg/kg per min) alone or combined. Each animal served as its own control. RIF BK and cGMP levels increased significantly over 1 h in response to valsartan, benazeprilat, or both but not to a vehicle control. The combined benazeprilat-valsartan effect was greater than the sum of their individual effects, suggesting potentiation rather than addition, and was abolished by PD 123,319. The authors demonstrate for the first time that an ACE inhibitor (benazepril) and an ARB (valsartan) potentiate each other, and the authors postulate that such combinations may be beneficial in clin. states marked by Ang II elevation, such as chronic heart failure, postinfarction left ventricular dysfunction, and **hypertension**.

REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L43 ANSWER 10 OF 16 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2000:337384 CAPLUS

TITLE: Patent focus on agents affecting cardiovascular and renal functions november 1999 - march 2000

AUTHOR(S): Lemmens-Gruber, Rosa

CORPORATE SOURCE: Institute of Pharmacology and Toxicology, University of Vienna, Vienna, A-1090, Austria

SOURCE: Expert Opinion on Therapeutic Patents (2000), 10(5), 533-548

CODEN: EOTPEG; ISSN: 1354-3776

PUBLISHER: Ashley Publications Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

ED Entered STN: 21 May 2000

AB Patent applications relevant to therapy of cardiovascular diseases are reviewed for the period of Nov. 1999 to Mar. 2000. Most of the patents discussed deal with agents affecting blood clotting, membrane ionic currents, **hypertension** and hypercholesterolemia. The development and evaluation of several new therapeutic agents for treatment of blood coagulation disorders are discussed, including glycoprotein (GP) IIb/IIIa antagonists, activators of protease-activated receptors, P2T **receptor antagonists**, adenosine receptor agonists and serine protease inhibitors. Interesting new blockers of the sodium-proton

exchange, the N-type calcium channels and the ultrarapid delayed rectifier potassium current (IKur) are introduced. Antihypertensive agents are presented including **angiotensin II receptor antagonists**, vasopressin antagonists and phosphodiesterase inhibitors. Compds. effective against hypercholesterolemia, especially inhibitors of cholesterol ester transfer protein (CETP) and acyl CoA:cholesterol acyltransferase (ACAT) are also addressed. Agents acting via other mechanisms, like the nitric oxide-**cGMP** (NO-**cGMP**) pathway, that are involved in cardiovascular effects are discussed.

REFERENCE COUNT: 86 THERE ARE 86 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L43 ANSWER 11 OF 16 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1999:370989 CAPLUS

DOCUMENT NUMBER: 131:168631

TITLE: Protective role of the angiotensin AT2 receptor in a renal wrap **hypertension** model

AUTHOR(S): Siragy, Helmy M.; Carey, Robert M.

CORPORATE SOURCE: Department of Medicine, University of Virginia Health Sciences Center, Charlottesville, VA, USA

SOURCE: Hypertension (1999), 33(5), 1237-1242

CODEN: HPRTDN; ISSN: 0194-911X

PUBLISHER: Lippincott Williams & Wilkins

DOCUMENT TYPE: Journal

LANGUAGE: English

ED Entered STN: 15 Jun 1999

AB We evaluated the role of the renal **angiotensin II** type 2 (AT2) receptor in blood pressure regulation in rats with 2-kidney, 1 figure-8 wrap (Grollman) **hypertension**. Renal wrapping increased systolic blood pressure (SBP). Renal interstitial fluid (RIF) bradykinin (BK), nitric oxide end-products (NOX), and **cGMP** were higher in the contralateral intact kidney than in the wrapped kidney. In rats with Grollman **hypertension**, losartan normalized SBP and increased renal function, RIF BK, NOX, and **cGMP** only in contralateral kidneys. In contrast, PD 123319, a specific AT2-**receptor antagonist**, significantly increased SBP and decreased RIF BK, NOX, and **cGMP** in both kidneys. Combined administration of losartan and PD 123319 prevented the decrease in SBP and the increase in RIF BK, NOX, and **cGMP** levels observed with losartan alone. BK-receptor blockade caused a significant increase in RIF BK and a decrease in RIF NOX and **cGMP** in both kidneys similar to that observed during administration of PD 123319. In rats that underwent sham operation, RIF BK increased in response to **angiotensin II**, an effect that was blocked by PD 123319. These data demonstrate that **angiotensin II** mediates renal production of BK, which, in turn, releases nitric oxide and **cGMP** via stimulation of AT2 receptors. The increase in blood pressure and the decrease in renal BK, nitric oxide, and **cGMP** during AT2-receptor blockade suggests that the AT2 receptor mediates counterregulatory vasodilation in Grollman **hypertension** and prevents a further increase in blood pressure.

REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L43 ANSWER 12 OF 16 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1999:1198 CAPLUS

DOCUMENT NUMBER: 130:204863

TITLE: Augmentation of the cardiac natriuretic peptides by beta-receptor antagonism: evidence from a population-based study

AUTHOR(S): Luchner, Andreas; Burnett, John C., Jr.; Jougasaki, Michihisa; Hense, Hans-Werner; Riegger, Gunter A. J.; Schunkert, Heribert

CORPORATE SOURCE: Klinik und Poliklinik fur Innere Medizin II,

SOURCE: University of Regensburg, Regensburg, D-93042, Germany
Journal of the American College of Cardiology (1998),
32(7), 1839-1844

CODEN: JACCDI; ISSN: 0735-1097

PUBLISHER: Elsevier Science Inc.

DOCUMENT TYPE: Journal

LANGUAGE: English

ED Entered STN: 04 Jan 1999

AB The present retrospective anal. of data derived from a population-based study examined the relationship between intake of **β -receptor antagonists** and plasma concns. of the cardiac natriuretic peptides and their second messenger. **β -Receptor antagonists** are widely used for treatment of cardiovascular disease. In addition to direct effects on heart rate and cardiac contractility, recent evidence suggests that **β -receptor antagonists** may also modulate the cross talk between the sympathetic nervous system and the cardiac natriuretic peptide system. Plasma concns. of atrial natriuretic peptide (ANP), brain natriuretic peptide (BNP) and their second messenger cyclic guanosine monophosphate (**cGMP**) were assessed in addition to anthropometric, hemodynamic and echocardiog. parameters in a population-based sample (n = 672), of which 80 subjects used **beta-receptor antagonists**. Compared to subjects without medication, subjects receiving **beta-receptor antagonists** were characterized by substantially elevated ANP, BNP and **cGMP** plasma concns. (plus 32%, 89% and 18%, resp., p < 0.01 each). Anal. of subgroups revealed that this effect was highly consistent and present even in the absence of **hypertension**, left atrial enlargement, left ventricular hypertrophy or left ventricular dysfunction. The most prominent increase was observed in a subgroup with increased left ventricular mass index. By multivariate anal., a statistically significant and independent association between **β -receptor antagonism** and ANP, BNP and **cGMP** concns. was confirmed. Such an association could not be demonstrated for other antihypertensive agents such as **angiotensin**-converting enzyme inhibitors or diuretics. **β -Receptor antagonists** appear to augment plasma ANP, BNP and **cGMP** concns. The current observation suggests an important contribution of the cardiac natriuretic peptide system to the therapeutic mechanism of **beta-receptor antagonists**.

REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L43 ANSWER 13 OF 16 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1998:91946 CAPLUS

DOCUMENT NUMBER: 128:191125

TITLE: AT2 receptor stimulation increases aortic cyclic GMP in SHRSP by a kinin-dependent mechanism

AUTHOR(S): Gohlke, Peter; Pees, Christiane; Unger, Thomas

CORPORATE SOURCE: Institute of Pharmacology, Christian-Albrechts University of Kiel and German Institute for High Blood Pressure Research, Heidelberg, Germany

SOURCE: Hypertension (1998), 31(1, Pt. 2), 349-355

CODEN: HPRTDN; ISSN: 0194-911X

PUBLISHER: Williams & Wilkins

DOCUMENT TYPE: Journal

LANGUAGE: English

ED Entered STN: 18 Feb 1998

AB In the present study we tested the hypothesis whether an **angiotensin** AT2 receptor-mediated stimulation of the bradykinin (BK)/nitric oxide (NO) system can account for the effects of AT1 receptor antagonism on aortic **cGMP** described previously in SHRSP. Adult SHRSP were treated for 4 h with **angiotensin** II (ANG II) (30 ng/kg per min i.v.) or vehicle (0.9% NaCl i.v.). Animals were pretreated with vehicle, losartan (100 mg/kg p.o.), PD 123319 (30 mg/kg i.v.), losartan plus PD 123319, icatibant (500 μ g/kg i.v.),

NG-nitro-L-arginine Me ester (L-NAME; 1 mg/kg i.v.), or minoxidil (3 mg/kg i.v.). Mean arterial blood pressure (MAP) was continuously monitored over the 4-h exptl. period, and plasma ANG II and aortic **cGMP** were measured by RIA at the end of the study. ANG II infusion over 4 h raised MAP by about 20 mm Hg. Losartan alone or losartan plus ANG II as well as minoxidil plus ANG II markedly reduced blood pressure when compared to vehicle-treated or ANG II-treated animals, resp. Plasma levels of ANG II were increased 2-fold by ANG II infusion alone or by ANG II in combination with icatibant, L-NAME, or minoxidil. The increase in plasma ANG II levels was even more pronounced after losartan treatment. Aortic **cGMP** content was significantly increased by ANG II, losartan, losartan plus ANG II, and minoxidil plus ANG II by 60%, 45%, 68%, and 52%, resp. The effects of ANG II and of losartan plus ANG II on aortic **cGMP** content were both blocked by cotreatment with the AT2 **receptor antagonist** PD 123319. Icatibant and L-NAME abolished the effects of ANG II on aortic **cGMP**. Our results demonstrate the following: (1) ANG II increases aortic **cGMP** by an AT2 receptor-mediated action because the effect could be prevented by an AT2 **receptor antagonist**; (2) the effect of ANG II was not secondary to blood pressure increase because it remained under reduction of MAP with minoxidil; (3) losartan increased aortic **cGMP** most likely by increasing plasma ANG II levels with a subsequent stimulation of AT2 receptor; and (4) the effects of AT2 receptor stimulation are mediated by BK and, subsequently, NO because they were abolished by B2 receptor blockade as well as by NO synthase inhibition.

REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L43 ANSWER 14 OF 16 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1997:24034 CAPLUS

DOCUMENT NUMBER: 126:69912

TITLE: Losartan reduces phenylephrine constrictor response in aortic rings from spontaneously **hypertensive** rats. Role of nitric oxide and angiotensin II type 2 receptors

AUTHOR(S): Maeso, Rosaura; Navarro-Cid, Josefa; Munoz-Garcia, Raquel; Rodrigo, Elena; Ruilope, Luis Miguel; Lahera, Vicente; Cachofeiro, Victoria

CORPORATE SOURCE: School Medicine, Complutense University, Madrid, 28040, Spain

SOURCE: Hypertension (Dallas) (1996), 28(6), 967-972
CODEN: HPRTDN; ISSN: 0194-911X

PUBLISHER: American Heart Association

DOCUMENT TYPE: Journal

LANGUAGE: English

ED Entered STN: 15 Jan 1997

AB Nitric oxide seems to be involved in the mechanisms underlying the antihypertensive and renal responses of losartan in spontaneously **hypertensive** rats (SHR). The authors investigated the contribution of nitric oxide to the effect of this **angiotensin** II (Ang II) type 1 (AT1) **receptor antagonist** on the constrictor response of phenylephrine in aortic rings from SHR. Furthermore, since it has been suggested that Ang II could bind to unblocked AT2 receptors, during administration of an AT1 **receptor antagonist**, the authors also studied the effect of the AT2 **receptor antagonist** PD 123319 on the contractile response to phenylephrine in aortic rings from SHR. To this end, dose-response curves of phenylephrine (10⁻⁹ to 10⁻⁵ mol/L) in the presence and absence of losartan (10⁻⁹, 10⁻⁷, and 10⁻⁵ mol/L) in SHR aortic rings were studied. Preincubation with losartan reduced the constrictor response to phenylephrine but not to KCl (10 to 120 mmol/L) in a dose-dependent manner. The presence of captopril (10⁻⁵ mol/L) in the incubation medium did not alter the response to phenylephrine, even at the dose of 10⁻³ mol/L. The reduced response to phenylephrine in the presence

of losartan was abolished in both endothelium-denuded rings and rings treated with a nitric oxide synthesis inhibitor. A similar situation was observed in PD 123319-pretreated rings, in which the effect of losartan on the contractile response to phenylephrine was reversed. Losartan was not able to stimulate the production of aortic **cGMP** compared with the control group. Likewise, losartan did not modify the relaxing responses to either acetylcholine or sodium nitroprusside in phenylephrine-precontracted aortic rings. Furthermore, losartan did not alter isometric tension in aortic rings in either basal or phenylephrine-precontracted conditions. These data demonstrate that Ang II potentiates the vasoconstriction induced by phenylephrine through the stimulation of AT1 receptors. Moreover, AT2 receptors and nitric oxide appear to be involved in this effect.

REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L43 ANSWER 15 OF 16 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1996:610907 CAPLUS

DOCUMENT NUMBER: 125:265483

TITLE: Cardiac and vascular effects of long-term losartan treatment in stroke-prone spontaneously **hypertensive** rats

AUTHOR(S): Gohlke, Peter; Linz, Wolfgang; Schoelkens, Bernward A.; Wiemer, Gabriele; Unger, Thomas

CORPORATE SOURCE: Department Pharmacology, Christian-Albrechts University Kiel, Kiel, 25601, Germany

SOURCE: Hypertension (Dallas) (1996), 28(3), 397-402
CODEN: HPRTDN; ISSN: 0194-911X

PUBLISHER: American Heart Association

DOCUMENT TYPE: Journal

LANGUAGE: English

ED Entered STN: 14 Oct 1996

AB In previous studies in stroke-prone spontaneously **hypertensive** rats (SHRSP), the authors demonstrated that early-onset, long-term **angiotensin**-converting enzyme inhibitor treatment improved cardiac function and metabolism and increased aortic **cGMP** content even at sub-antihypertensive doses. These effects could be prevented by bradykinin type 2 (B2) receptor blockade with icatibant. In the present study, the authors studied the effects of long-term oral treatment with the **angiotensin** type 1 (AT1) **receptor antagonist** losartan (30 mg/kg per day) on functional and biochem. parameters of the heart and on **cGMP** content in the aorta in SHRSP treated prenatally and subsequently up to the age of 20 wk. Losartan prevented the development of **hypertension** and left ventricular hypertrophy. Cardiac function measured ex vivo in isolated perfused hearts was improved, as demonstrated by significant increases in left ventricular pressure (22.4%), differentiated left ventricular pressure (dP/dtmax) (35.1%), and coronary flow (38%). The release of the intracellular enzymes lactate dehydrogenase and creatine kinase and of lactate into the coronary effluent was reduced by 46.4%, 47.2%, and 63.6%, resp. In myocardial tissue, the concns. of glycogen and the energy-rich phosphates ATP and creatine phosphate were increased by 43.2%, 33.1%, and 42.4%, resp., whereas lactate was decreased by 57.0%. The aortic tissue content of **cGMP** was increased fivefold. The results demonstrate that chronic blockade of AT1 receptors with losartan improved cardiac function and metabolism and increased aortic **cGMP** content in SHRSP to an extent similar to that observed previously after long-term **angiotensin**-converting enzyme inhibitor treatment at a comparably antihypertensive dose. Prevention of **hypertension** and cardiac hypertrophy as well as stimulation of non-AT1 receptors are discussed to explain the cardiac and vascular actions of losartan.

L43 ANSWER 16 OF 16 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1996:53963 CAPLUS

DOCUMENT NUMBER: 124:164765
TITLE: Chronic low-dose treatment with perindopril improves
cardiac function in stroke-prone spontaneously
hypertensive rats by potentiation of
endogenous bradykinin
AUTHOR(S): Gohlke, Peter; Unger, Thomas
CORPORATE SOURCE: Department Pharmacology, Christian Albrechts
University Kiel, Kiel, 424105, Germany
SOURCE: American Journal of Cardiology (1995), 76(15), 41E-5E
CODEN: AJCDAG; ISSN: 0002-9149
PUBLISHER: Excerpta Medica
DOCUMENT TYPE: Journal
LANGUAGE: English

ED Entered STN: 26 Jan 1996

AB The authors investigated the effect of chronic **angiotensin**
-converting enzyme (ACE) inhibitor treatment on functional and biochem.
cardiac parameters in stroke-prone spontaneously **hypertensive**
rats (SHRsp). Animals were treated prenatally and, subsequently, up to
the age of 20 wk with the ACE inhibitor perindopril (0.01 and 1 mg/kg per
day). The contribution of endogenous bradykinin potentiation to the
actions of the ACE inhibitor was assessed by co-treatment with the
bradykinin **B2-receptor antagonist**, icatibant (500
µg/kg/day s.c.), from 6 to 20 wk of age and by measurement of
myocardial prostacyclin and **cGMP** concns. Chronic high-dose
treatment with perindopril attenuated the development of
hypertension and left ventricular hypertrophy while low-dose
perindopril treatment had no effect on these parameters. However,
low-dose perindopril improved cardiac function of isolated perfused hearts
as demonstrated by an increasing left ventricular pressure and dp/dtmax
without change in heart rate. Low-dose perindopril further reduced
lactate concns. and the enzymic activities of lactate dehydrogenase and
creatine kinase in the coronary venous effluent and increased tissue
concns. of glycogen, ATP, and creatine kinase in the myocardium.
Concomitant chronic bradykinin receptor blockade abolished all ACE
inhibitor-induced effects on cardiac function and metabolism. Cardiac
prostacyclin concns. were 3-fold elevated in perindopril-treated animals
when compared to vehicle-treated controls, while cardiac **cGMP**
concns. remained unchanged. The data demonstrate that chronic ACE
inhibitor treatment can improve cardiac function and metabolism independently
of the antihypertensive and antihypertrophic drug actions by potentiation
of endogenous bradykinin.

=> d his

(FILE 'HOME' ENTERED AT 11:49:08 ON 02 MAR 2005)

FILE 'CAPLUS' ENTERED AT 11:49:13 ON 02 MAR 2005

E FOX DAVID/AU
L1 69 S E2-E3, E20-E22
E HUGHES BERNADETTE/AU
L2 22 S E3-E4
E HUGHES B/AU
L3 40 S E3
E FOX D/AU
E FOX D?/AU
E FOX D/AU
L4 75 S E3
L5 144 S L1 OR L4
L6 62 S L2 OR L3
L7 204 S L5 OR L6
L8 10 S L7 AND HYPERTENSI?
L9 0 S L7 AND (CYCLIC GUANOSINE MONOPHOSPHATE (W) (PHOSPHODIESTERASE
L10 6 S L7 AND ("CGMP" OR "PDE5" OR "ANGIOTENSIN II RECEPTOR ANTAGONI

FILE 'REGISTRY' ENTERED AT 11:57:43 ON 02 MAR 2005

L11 2 S E3-E4
 E SILDENAFIL/CN
L12 1 S E3
 E TADALAFIL/CN
L13 3 S E3-E5
L14 1 S CANDESARTAN/CN
 E CANDESARTAN/CN
L15 2 S E3-E5
 E EPROSARTAN/CN
L16 2 S E3-E5
 E IRBESARTAN/CN
L17 4 S E3-E6
 E LOSARTAN/CN
L18 4 S E3-E7
 E OLMESARTAN/CN
L19 2 S E3-E5
 E SARALASIN/CN
L20 2 S E3-E4
 E TELMISARTAN/CN
L21 5 S E3-E7
 E VALSARTAN/CN
L22 2 S E3-E4
L23 6 S L11 OR L12 OR L13
L24 23 S L15 OR L16 OR L17 OR L18 OR L19 OR L20 OR L21 OR L22

FILE 'CAPLUS' ENTERED AT 12:02:01 ON 02 MAR 2005

L25 1081 S L23
L26 4320 S L24
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L27 78751 S E3, E16
 E HYPERTENSION/CT
L28 43383 S E3
L29 78751 S L27 OR L28
L30 80818 S L29 OR (HIGH BLOOD PRESSURE) OR (ELEVATED BLOOD PRESSURE) OR
L31 36 S L25 AND L26
L32 9 S L31 (L) L30
L33 9 S L30 AND L31
L34 34 S L25 (L) L30
L35 1025 S L26 (L) L30
L36 0 S L34 AND L35
L37 9 S L31 AND HYPERTENS?
L38 0 S L37 NOT L33
L39 20335 S "CGMP" OR "PDE5" OR (CYCLIC GUANOSINE MONOPHOSPHATE (W) PHOSP
L40 6539 S (ANGIOTENSIN (L) RECEPTOR ANTAGONIST) OR (ANGIOTENSIN RECEPTO
L41 80 S L39 (L) L40
L42 17 S L41 AND HYPERTENS?
L43 16 S L42 NOT L33

=> d cost

COST IN U.S. DOLLARS

	SINCE FILE	TOTAL
	ENTRY	SESSION
CONNECT CHARGES	8.58	16.78
NETWORK CHARGES	1.32	2.64
SEARCH CHARGES	56.70	254.68
DISPLAY CHARGES	66.25	108.65
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FULL ESTIMATED COST	132.85	382.75

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

	SINCE FILE	TOTAL
	ENTRY	SESSION
CA SUBSCRIBER PRICE	-18.25	-29.93

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L44 115 L31 OR L41

=> s 144 and (angina? or stroke? or diabet? or congestive heart failure?)

8156 ANGINA?

25215 STROKE?

109357 DIABET?

6780 CONGESTIVE

300773 HEART

26101 HEARTS

302455 HEART

(HEART OR HEARTS)

174094 FAILURE?

6178 CONGESTIVE HEART FAILURE?

(CONGESTIVE(W) HEART(W) FAILURE?)

L45 15 L44 AND (ANGINA? OR STROKE? OR DIABET? OR CONGESTIVE HEART FAILURE?)

=> s 145 not 143

L46 11 L45 NOT L43

=> s 146 not 133

L47 6 L46 NOT L33

=> d 147 1-6 ibib ed abs

L47 ANSWER 1 OF 6 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:878382 CAPLUS

DOCUMENT NUMBER: 141:350161

TITLE: Preparation of azole compounds as PTP1B inhibitors

INVENTOR(S): Ikemoto, Tomoyuki; Tanaka, Masahiro; Yuno, Takeo; Sakamoto, Johei; Nakanishi, Hiroyuki; Nakagawa, Yuichi; Ohta, Takeshi; Sakata, Shohei; Morinaga, Hisayo

PATENT ASSIGNEE(S): Japan Tobacco Inc., Japan

SOURCE: PCT Int. Appl., 542 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004089918	A1	20041021	WO 2004-JP5119	20040409
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			

PRIORITY APPLN. INFO.:

JP 2003-105267

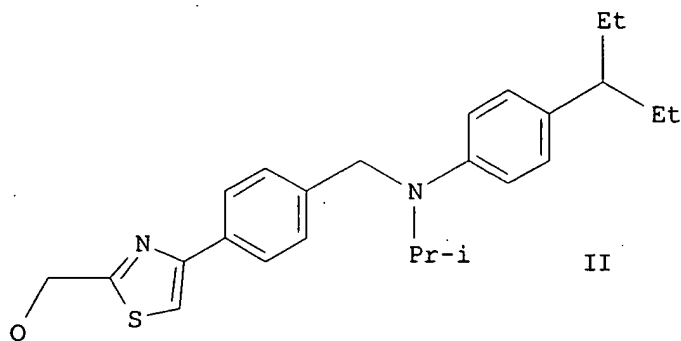
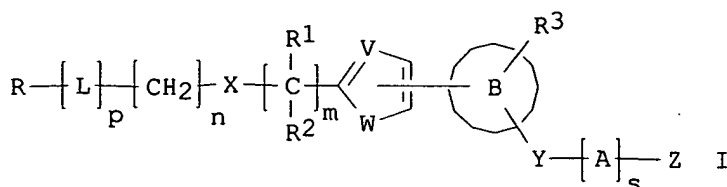
A 20030409

JP 2003-157590

A 20030603

OTHER SOURCE(S): MARPAT 141:350161

ED Entered STN: 22 Oct 2004



AB Title compds. I [V = N, CH; W = S, O; m = 0-2; R¹, R² = H, alkyl; X = NR⁴, etc.; R⁴ = H, alkyl; n = 0-4; p = 0, 1; L = CR²⁰R²¹, etc.; R²⁰ = H, alkyl, etc.; R²¹ = H, alkyl, etc.; R = CO²R¹⁹, etc.; R¹⁹ = H, alkyl; B = aryl, heteroaryl; R³ = H, halo, etc.; Y = O, etc.; s = 0, 1; A = (un)substituted alkylene with cycloalkyl; Z = cycloalkyl, etc.] were prepared. For example, O-alkylation of 5-hydroxynicotinic acid Me ester with compound II [Q = Cl], e.g., prepared from 4-bromoacetylbenzoic acid in 5 steps, followed by

saponification

afforded compound II [3-carboxypyridin-5-yloxy] in 44.1% overall yield. In PTP1B (protein tyrosine phosphatase 1B) inhibition assays, the IC₅₀ value of compound II [Q = 3-carboxypyridin-5-yloxy] was 0.28 μM. Compds. I are claimed useful for the treatment of obesity, **diabetes**, etc. Formulations are given.

REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L47 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2003:154230 CAPLUS

DOCUMENT NUMBER: 138:210277

TITLE: Synthesis and use of reagents for improved DNA lipofection and/or slow release prodrug and drug therapies

INVENTOR(S): Diamond, Scott L.; Gruneich, Jeffrey

PATENT ASSIGNEE(S): The Trustees of the University of Pennsylvania, USA

SOURCE: PCT Int. Appl., 70 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003015757	A1	20030227	WO 2002-US26152	20020815
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,				

CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,
UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU,
TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG,
CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,
PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR,
NE, SN, TD, TG

EP 1424998 A1 20040609 EP 2002-759383 20020815

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK

PRIORITY APPLN. INFO.:

US 2001-312729P P 20010816
US 2002-358138P P 20020220
WO 2002-US26152 W 20020815

ED Entered STN: 28 Feb 2003

AB The invention relates to compns. and methods for a one-step synthetic technique for making cationic steroid or cationic drug mols. for use as delivery vehicles. The invention further relates to methods for using cationic steroid mols. in lipofection or transfection, delivery of drugs, and for treatment of inflammation and other diseases and disorders. The invention also relates to cationic steroid prodrugs and cationic prodrugs and to methods of modifying drugs.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L47 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2001:431177 CAPLUS

DOCUMENT NUMBER: 135:162931

TITLE: Angiotensin regulates endothelin-B receptor in rat inner medullary collecting duct

AUTHOR(S): Wong, Norman L. M.; Tsui, Joseph K. C.

CORPORATE SOURCE: Department of Medicine, University of British Columbia, Vancouver, BC, Can.

SOURCE: Metabolism, Clinical and Experimental (2001), 50(6), 661-666

CODEN: METAAJ; ISSN: 0026-0495

PUBLISHER: W. B. Saunders Co.

DOCUMENT TYPE: Journal

LANGUAGE: English

ED Entered STN: 14 Jun 2001

AB The authors' recent studies showed that endothelin (ET)B receptors are downregulated in **congestive heart failure**. These changes in ETB receptor d. can be prevented by **angiotensin**-converting enzyme inhibitors, suggesting a possible role for **angiotensin**. Using isolated inner medullary collecting ducts (IMCD), the authors examined the possibility that **angiotensin**-induced downregulation of ETB receptors is accompanied by a decrease in ETB receptor mRNA. Binding studies showed that overnight incubation with **angiotensin** II induced a downregulation of ETA and ETB receptors' d. in IMCD by 39% and 29%, resp. This downregulation in ET receptor d. was abolished when IMCD was coincubated with **angiotensin** II and its **receptor antagonist** saralasin. Furthermore, when the cells were exposed to phorbol myristate acetate (PMA), it resulted in a reduction in ETA and ETB receptor binding sites by 41% and 34%, resp., suggesting the involvement of protein kinase C (PKC). In isolated IMCD, ET-1 induced an increase in cyclic guanosine monophosphate (**cGMP**) accumulation (705 ± 63 to $1,015 \pm 88$ fmol/ μ g protein/5min, $P < .01$), and the ET-1-induced accumulation was attenuated in the presence of **angiotensin** II (641 ± 45 to 809 ± 46 fmol/ μ g protein/5min, $P < .01$). Using competitive PCR method, the authors also observed downregulation of ETA and ETB receptors mRNA in IMCD treated with **angiotensin** II (1.09 ± 0.11 v 0.77 ± 0.07 amol/ μ g of

total RNA, $P < .01$; ETB, 14.80 ± 1.95 v 8.65 ± 0.67 amol/ μ g of total RNA, $P < .01$). The addition of a PKC inhibitor abolished the downregulation of ETA and ETB receptor mRNA induced by **angiotensin II** (ETA, 1.25 ± 0.07 v 1.19 ± 0.06 amol/ μ g of total RNA, not significant [NS]; ETB, 14.36 ± 0.83 to 13.68 ± 0.64 amol/ μ g of total RNA, NS). These results suggest that **angiotensin II**-induced downregulation of ETA and ETB receptors mRNA is mediated by a mechanism involving PKC.

REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L47 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2000:204037 CAPLUS

DOCUMENT NUMBER: 132:216831

TITLE: Angiotensin II type 1 receptor antagonist decreases plasma levels of tumor necrosis factor alpha, interleukin-6 and soluble adhesion molecules in patients with chronic heart failure

AUTHOR(S): Tsutamoto, Takayoshi; Wada, Atsuyuki; Maeda, Keiko; Mabuchi, Naoko; Hayashi, Masaru; Tsutsui, Takashi; Ohnishi, Masato; Sawaki, Masahide; Fujii, Masanori; Matsumoto, Takehiro; Kinoshita, Masahiko

CORPORATE SOURCE: First Department of Internal Medicine, Shiga University of Medical Science, Otsu, Japan

SOURCE: Journal of the American College of Cardiology (2000), 35(3), 714-721

CODEN: JACCDI; ISSN: 0735-1097

PUBLISHER: Elsevier Science Inc.

DOCUMENT TYPE: Journal

LANGUAGE: English

ED Entered STN: 30 Mar 2000

AB OBJECTIVES: To evaluate the effects of an **angiotensin** (Ang II) type 1 **receptor antagonist** on immune markers in patients with **congestive heart failure** (CHF). BACKGROUND: Ang II stimulates production of immune factors via the Ang II type 1 receptor in vitro, and the long-term effects of Ang II type 1 **receptor antagonists** on plasma markers of immune activation are unknown in patients with CHF. METHODS: Twenty-three patients with mild to moderate CHF with left ventricular dysfunction were randomly divided into two groups: treatment with Ang II type 1 receptor (candesartan cilexetil) ($n = 14$) or placebo ($n = 9$). We measured plasma levels of immune factors such as tumor necrosis factor alpha (TNFalpha), interleukin-6 (IL-6), soluble intercellular adhesion mol.-1 (sICAM-1) and soluble vascular cell adhesion mol.-1 (sVCAM-1). We also measured plasma levels of the neurohumoral factors such as atrial natriuretic peptide (ANP) and brain natriuretic peptide (BNP) and **cGMP** (**cGMP**), a biol. marker of ANP and BNP. RESULTS: Plasma levels of TNFalpha, IL-6, sICAM-1 and sVCAM-1 were increased in the 23 CHF patients compared with normal subjects and significantly decreased after 14 wk of candesartan cilexetil treatment, but did not change in the placebo group. Plasma levels of BNP, which is a marker of ventricular injury, significantly decreased, and the molar ratio of plasma **cGMP** to cardiac natriuretic peptides (ANP + BNP) was significantly increased after candesartan cilexetil treatment, but did not change in the placebo group. CONCLUSIONS: These findings suggest that 14 wk of treatment with an Ang II type 1 **receptor antagonist** (candesartan cilexetil) decreased plasma levels of the immune markers such as TNFalpha, IL-6, sICAM-1 and sVCAM-1 and that it improved the biol. compensatory action of endogenous cardiac natriuretic peptides in patients with mild to moderate CHF.

REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L47 ANSWER 5 OF 6 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1997:778166 CAPLUS

DOCUMENT NUMBER: 128:60216

TITLE: Impaired nitric oxide-mediated renal vasodilation in rats with experimental heart failure; role of angiotensin II

AUTHOR(S): Abassi, Zaid A.; Gurbanov, Konstantin; Mulroney, Susan E.; Potlog, Clariss; Opgenorth, Terry J.; Hoffman, Aaron; Haramati, Aviad; Winaver, Joseph

CORPORATE SOURCE: Department of Physiology and Biophysics, Faculty of Medicine, Technion, Haifa, Israel

SOURCE: Circulation (1997), 96(10), 3655-3664

CODEN: CIRCAZ; ISSN: 0009-7322

PUBLISHER: American Heart Association

DOCUMENT TYPE: Journal

LANGUAGE: English

ED Entered STN: 13 Dec 1997

AB **Congestive heart failure (CHF)** is associated with a decrease in renal perfusion. Because endothelium-derived NO is important in the regulation of renal blood flow (RBF), the authors tested the hypothesis that an impairment in the NO system may contribute to the decrease in RBF in rats with exptl. CHF. Studies were performed in rats with exptl. high-output CHF induced by aortocaval (AV) fistula and sham-operated controls. In controls, incremental doses of acetylcholine (ACh, 1 to 100 µg/kg/min) increased RBF and caused a dose-related decrease in renal vascular resistance (RVR). However, the increase in RBF and decrease in RVR were markedly attenuated in rats with CHF. Likewise, the effects of ACh on urinary sodium and **cGMP** excretion were also diminished in CHF rats, as was the renal vasodilatory effect of the NO donor S-nitroso-N-acetylpenicillamine (SNAP). These attenuated responses to endothelium-dependent and -independent renal vasodilators in CHF rats occurred despite a normal baseline and stimulated NO₂+NO₃ excretion and normal expression of renal endothelial NO synthase (eNOS), as determined by eNOS mRNA levels and immunoreactive protein. Infusion of the NO precursor L-arginine did not affect baseline RBF or the response to ACh in rats with CHF. However, administration of the nonpeptide **angiotensin II receptor antagonist**

A81988 before ACh completely restored the renal vasodilatory response to ACh in CHF rats. This study demonstrates that despite a significant attenuation in the NO-related renal vasodilatory responses, the integrity of the renal NO system is preserved in rats with chronic AV fistula. This impairment in NO-mediated renal vasodilation in exptl. CHF appears to be related to increase activity of the renin-**angiotensin** system and may contribute further to the decrease in renal perfusion seen in CHF.

REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L47 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1997:351367 CAPLUS

DOCUMENT NUMBER: 127:63989

TITLE: Chronic effects of ANG II antagonist in heart failure: improvement of cGMP generation from ANP

AUTHOR(S): Maeda, Yukiharu; Wada, Atsuyuki; Tsutamato, Takayoshi; Fukai, Daisuke; Kinoshita, Masahiko

CORPORATE SOURCE: First Department of Internal Medicine, Shiga University of Medical Science, Ohtsu, 520-21, Japan

SOURCE: American Journal of Physiology (1997), 272(5, Pt. 2), H2139-H2145

CODEN: AJPHAP; ISSN: 0002-9513

PUBLISHER: American Physiological Society

DOCUMENT TYPE: Journal

LANGUAGE: English

ED Entered STN: 05 Jun 1997

AB To evaluate the effects of endogenous **angiotensin II (ANG II)** on the development of **congestive heart failure**

(CHF), we examined cardiorenal and hormonal factors after chronic administration of the ANG II type 1 **receptor antagonist**

TCV-116 in dogs with CHF induced by rapid right ventricular pacing. After 8 days of pacing, TCV-116 administration [1 (group 1) or 3 mg·kg⁻¹·day⁻¹ (group 2)] was started and continued until the 22nd day. TCV-116 was found to have protected the deterioration of cardiorenal functions and the activation of neurohormonal factors. Although there was no significant difference in the pulmonary capillary wedge pressure or plasma atrial natriuretic peptide (ANP) level between the TCV-116-treated groups (354 ± 85 and 364 ± 29 pg/mL for groups 1 and 2, resp.) and the vehicle group (385 ± 20 pg/mL), the plasma guanosine 3',5'-cyclic monophosphate (**cgmp**) levels, a second messenger of ANP, were twofold higher in TCV-116-treated groups (49.4 ± 10.2 and 50.6 ± 7.7 pmol/mL for groups 1 and 2, resp.) than in the vehicle group (24 ± 4.0 pmol/mL), with a high correlation between the plasma ANP and **cgmp** levels (r = 0.90; P < 0.05). These findings indicate that endogenous ANG II has important roles in hemodynamics and renal functions during the development of CHF, which may be due, in part, to a reduction in endogenous ANP activity, suggesting the usefulness of an ANG II-**receptor antagonist** against the development of CHF.

REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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(FILE 'HOME' ENTERED AT 11:49:08 ON 02 MAR 2005)

FILE 'CAPLUS' ENTERED AT 11:49:13 ON 02 MAR 2005

	E FOX DAVID/AU
L1	69 S E2-E3, E20-E22
	E HUGHES BERNADETTE/AU
L2	22 S E3-E4
	E HUGHES B/AU
L3	40 S E3
	E FOX D/AU
	E FOX D?/AU
	E FOX D/AU
L4	75 S E3
L5	144 S L1 OR L4
L6	62 S L2 OR L3
L7	204 S L5 OR L6
L8	10 S L7 AND HYPERTENSI?
L9	0 S L7 AND (CYCLIC GUANOSINE MONOPHOSPHATE (W) (PHOSPHODIESTERASE
L10	6 S L7 AND ("CGMP" OR "PDE5" OR "ANGIOTENSIN II RECEPTOR ANTAGONI

FILE 'REGISTRY' ENTERED AT 11:57:43 ON 02 MAR 2005

	E SILDENAFIL/CN
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	E TADALAFIL/CN
L12	1 S E3
	E VARDENAFIL/CN
L13	3 S E3-E5
L14	1 S CANDESARTAN/CN
	E CANDESARTAN/CN
L15	2 S E3-E5
	E EPROSARTAN/CN
L16	2 S E3-E5
	E IRBESARTAN/CN
L17	4 S E3-E6
	E LOSARTAN/CN
L18	4 S E3-E7
	E OLMESARTAN/CN
L19	2 S E3-E5

L20 E SARALASIN/CN
2 S E3-E4

L21 E TELMISARTAN/CN
5 S E3-E7
E VALSARTAN/CN

L22 2 S E3-E4

L23 6 S L11 OR L12 OR L13

L24 23 S L15 OR L16 OR L17 OR L18 OR L19 OR L20 OR L21 OR L22

FILE 'CAPLUS' ENTERED AT 12:02:01 ON 02 MAR 2005

L25 1081 S L23

L26 4320 S L24
E HYPERTENSION/BI

L27 78751 S E3, E16
E HYPERTENSION/CT

L28 43383 S E3

L29 78751 S L27 OR L28

L30 80818 S L29 OR (HIGH BLOOD PRESSURE) OR (ELEVATED BLOOD PRESSURE) OR

L31 36 S L25 AND L26

L32 9 S L31 (L) L30

L33 9 S L30 AND L31

L34 34 S L25 (L) L30

L35 1025 S L26 (L) L30

L36 0 S L34 AND L35

L37 9 S L31 AND HYPERTENS?

L38 0 S L37 NOT L33

L39 20335 S "CGMP" OR "PDE5" OR (CYCLIC GUANOSINE MONOPHOSPHATE (W) PHOSP

L40 6539 S (ANGIOTENSIN (L) RECEPTOR ANTAGONIST) OR (ANGIOTENSIN RECEPTO

L41 80 S L39 (L) L40

L42 17 S L41 AND HYPERTENS?

L43 16 S L42 NOT L33

L44 115 S L31 OR L41

L45 15 S L44 AND (ANGINA? OR STROKE? OR DIABET? OR CONGESTIVE HEART FA

L46 11 S L45 NOT L43

L47 6 S L46 NOT L33

=> s 146 not 147

L48 5 L46 NOT L47

=> d 148 1-5 ibib ed abs

L48 ANSWER 1 OF 5 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2005:77981 CAPLUS

DOCUMENT NUMBER: 142:162662

TITLE: Nanoparticulate glipizide compositions

INVENTOR(S): Bosch, H. William; Ryde, Niels P.

PATENT ASSIGNEE(S): Elan Pharma International Limited, USA

SOURCE: U.S. Pat. Appl. Publ., 24 pp., Cont.-in-part of U.S. Ser. No. 276,400.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 16

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005019412	A1	20050127	US 2003-701064	20031105
US 2002012675	A1	20020131	US 1999-337675	19990622
WO 2001087264	A2	20011122	WO 2001-US15983	20010518
WO 2001087264	A3	20020620		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,

LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT,
RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US,

UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

US 2004013613 A1 20040122 US 2003-276400 20030115
PRIORITY APPLN. INFO.: US 1998-164351 B2 19981001
US 1999-337675 A2 19990622
WO 2001-US15983 W 20010518
US 2003-276400 A2 20030115
US 2000-572961 A 20000518

ED Entered STN: 28 Jan 2005

AB The present invention is directed to nanoparticulate compns. comprising
glipizide. The glipizide particles of the composition preferably have an
effective average particle size of <2 μ . Thus, a formulation contained
spray-dried glipizide 5.33, mannitol 13.47, xylitol 40.53, citric acid
19.60, sodium bicarbonate 19.33, Asparatme 0.28, PEG-4000 0.93, and sodium
stearyl fumarate 0.53%.

L48 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:759835 CAPLUS

DOCUMENT NUMBER: 141:277616

TITLE: Preparation of 3-(1-[3-(1,3-benzothiazol-6-
yl)propylcarbamoyl]cycloalkyl)propanoic acid
derivatives as nep inhibitors

INVENTOR(S): Hepworth, David

PATENT ASSIGNEE(S): Pfizer Inc., UK

SOURCE: U.S. Pat. Appl. Publ., 27 pp., which

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004180941	A1	20040916	US 2004-800065	20040312
WO 2004080985	A1	20040923	WO 2004-IB822	20040309
W:				
AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,				
CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,				
GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,				
LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,				
NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,				
TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW:				
BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ,				
BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE,				
ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI,				
SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN,				
TD, TG				

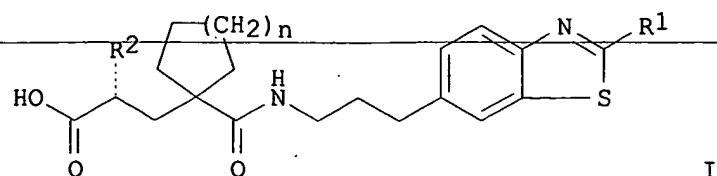
NL 1025709 A1 20040916 NL 2004-1025709 20040312

PRIORITY APPLN. INFO.: GB 2003-5916 A 20030314
US 2003-464608P P 20030422
GB 2003-29143 A 20031216
US 2004-538079P P 20040120

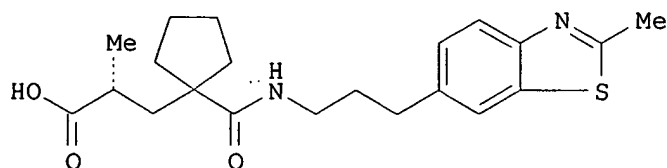
OTHER SOURCE(S): MARPAT 141:277616

ED Entered STN: 17 Sep 2004

GI



I



II

AB The invention relates to the use of title compds. I [R1 = H or Me; R2 = Me or Et; n = 1 or 2] as inhibitors of neutral endopeptidase enzyme (NEP), processes for the preparation thereof, intermediates used in the preparation thereof and compns. containing said inhibitors. Thus, e.g., II was prepared by amidation of 1-[(2R)-3-tert-butoxy-2-methyl-3-oxopropyl]cyclopentane carboxylic acid with 3-(2-methyl-1,3-benzothiazol-6-yl)propylamine dihydrochloride (preparation given) with subsequent hydrolysis to provide the free acid. I have been demonstrated to possess IC50 values of <20 nanomolar in tests for NEP inhibition and demonstrate a selectivity over soluble secreted endopeptidase (SEP) of at least 1000 fold. These inhibitors have utility in a variety of therapeutic areas including the treatment of male and female sexual dysfunction, particularly female sexual dysfunction (FSD), especially wherein the FSD is female sexual arousal disorder (FSAD).

L48 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:269863 CAPLUS

DOCUMENT NUMBER: 140:281417

TITLE: Combination therapy using antihypertensive agents and endothelin antagonists for vascular conditions associated with a male or female sexual dysfunction
INVENTOR(S): Adams, Michael A.; Hale, Taben M.; Heaton, Jeremy P. W.

PATENT ASSIGNEE(S): Queen's University At Kingston, Can.; Callegy Pharmaceuticals, Inc.

SOURCE: U.S. Pat. Appl. Publ., 29 pp., Cont.-in-part of U.S. Pat. Appl. 2003 8,020.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004063719	A1	20040401	US 2003-429197	20030502
US 6284763	B1	20010904	US 1999-382749	19990825
US 2002035067	A1	20020321	US 2001-902787	20010712
US 6458797	B2	20021001		
US 2003008020	A1	20030109	US 2002-192281	20020709
US 6787553	B2	20040907		
US 2004234619	A1	20041125	US 2004-869755	20040615
PRIORITY APPLN. INFO.:			US 1998-98178P	P 19980826
			US 1999-382749	A1 19990825
			US 2001-902787	A1 20010712
			US 2002-377917P	P 20020502

ED Entered STN: 02 Apr 2004

AB The present invention provides a method for a more efficacious treatment of a vascular condition through the administration of a therapeutically effective amount of a combination of an anti-pressor agent, an endothelin antagonist, and a sex hormone for repetitive cycles of on/off-treatment. In one embodiment, the invention provides a method for the prevention of tolerance induced by an anti-pressor agent via the inclusion of an endothelin antagonist in a combination therapy approach to remodel vascular structure and treat vascular conditions associated with a male or female sexual dysfunction, atherosclerosis, renal failure, hypertension, congestive heart failure, diabetic nephropathy, and diabetic neuropathy. The anti-pressor agent comprises one or more compds. such as prostaglandin-E 1, an ACE inhibitor, an angiotensin-II receptor antagonist, an α 1-adrenergic receptor antagonist, a β -adrenergic receptor antagonist, a calcium channel blocker, an activator of guanylyl cyclase or adenylyl cyclase, a phosphodiesterase inhibitor, and hydralazine. The endothelin antagonist comprises one or more compds. such as a peptidal endothelin antagonist, a non-peptidal endothelin antagonist, and an inhibitor of endothelin converting enzyme. Such a combination therapy approach enhances the efficacy of the anti-pressor agent and enables an increase in the frequency and duration of anti-pressor administrations for the long term treatment of vascular conditions.

L48 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:60341 CAPLUS

DOCUMENT NUMBER: 140:117406

TITLE: Liquid dosage compositions of stable nanoparticulate drugs

INVENTOR(S): Bosch, William H.; Hilborn, Matthew R.; Hovey, Douglas C.; Kline, Laura J.; Lee, Robert W.; Pruitt, John D.; Ryde, Niels P.; Ryde, Tuula A.; Xu, Shuqian

PATENT ASSIGNEE(S): Elan Pharma International, Ltd, Ire.

SOURCE: PCT Int. Appl., 68 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 16

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004006959	A1	20040122	WO 2003-US22187	20030716
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				

PRIORITY APPLN. INFO.:

US 2002-396530P

P 20020716

ED Entered STN: 26 Jan 2004

AB The present invention relates to liquid dosage compns. of stable nanoparticulate drugs. The liquid dosage compns. of the invention include osmotically active crystal growth inhibitors that stabilize the nanoparticulate active agents against crystal and particle size growth of the drug. Thus, an aqueous nanoparticulate colloidal dispersion (NCD) comprising drug 32.5 Copovidone 6.5, and dioctyl sodium sulfosuccinate 0.464% by weight was prepared by milling for 3.8 h under high energy milling conditions. The final mean particle size (by weight) of the drug particles

was 161 nm. The concentrated NCD was then diluted with preserved water and glycerol (the osmotically active crystal growth inhibitor) to 0.5-3.0% drug.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L48 ANSWER 5 OF 5 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2003:396889 CAPLUS

DOCUMENT NUMBER: 138:401744

TITLE: Preparation of polycyclic guanine derivative phosphodiesterase V inhibitors

INVENTOR(S): Asberom, Theodoros; Clader, John W.; Hu, Yueqing; Pissarnitski, Dmitri A.; Stamford, Andrew W.; Xu, Ruo

PATENT ASSIGNEE(S): Schering Corporation, USA

SOURCE: PCT Int. Appl., 95 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003042216	A1	20030522	WO 2002-US35721	20021107
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LU, LV, MA, MD, MG, MK, MN, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SC, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UZ, VC, VN, YU, ZA, ZM			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
US 2003176413	A1	20030918	US 2002-290011	20021107
EP 1442042	A1	20040804	EP 2002-786685	20021107
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK			
PRIORITY APPLN. INFO.:			US 2001-344498P	P 20011109
			WO 2002-US35721	W 20021107

OTHER SOURCE(S): MARPAT 138:401744

ED Entered STN: 23 May 2003

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. I [q = 0-2; R1, R3-6 = H, alkyl, aryl, heteroaryl, cycloalkyl, heterocycloalkyl; R2 = H, halo, alkyl, alkoxy, etc.; Y = alkyl, aryl] are prepared For instance, 4-amino-1-benzyl-5-(ethoxycarbonyl)imidazole (preparation given) is treated with ethylisocyanate (o-xylene, reflux, 16 h), the resulting product cyclized (MeOH, NaOMe, reflux, 4 h), subsequently treated with POCl3 and the product used to alkylate (R)-2-amino-3-phenylpropanol (NMP, 130°, 12 h) which provides II. II is treated with MsCl (Et3N), debenzylated (MeOH, NH4O2CH, Pd(OH)2/C, reflux, 3 h), brominated (HOAc, NaOAc, Br2), alkylated with 3-chloro-4-methoxybenzyl bromide (DMF, K2CO3) and treated with NaOEt (DMF/EtOH) to afford III. III has IC50 < 4.1 nM for PDE V and IC50 > 300 nM for PDE VI. I are useful for treating sexual dysfunction.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d cost

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

	ENTRY	SESSION
CONNECT CHARGES	10.92	19.12
NETWORK CHARGES	1.68	3.00
SEARCH CHARGES	68.04	266.02
DISPLAY CHARGES	95.40	137.80

FULL ESTIMATED COST	176.04	425.94
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	SINCE FILE	TOTAL
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	ENTRY	SESSION
CA SUBSCRIBER PRICE	-26.28	-37.96

IN FILE 'CAPLUS' AT 12:19:01 ON 02 MAR 2005

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(FILE 'HOME' ENTERED AT 11:49:08 ON 02 MAR 2005)

FILE 'CAPLUS' ENTERED AT 11:49:13 ON 02 MAR 2005

	E FOX DAVID/AU
L1	69 S E2-E3, E20-E22
	E HUGHES BERNADETTE/AU
L2	22 S E3-E4
	E HUGHES B/AU
L3	40 S E3
	E FOX D/AU
	E FOX D?/AU
	E FOX D/AU
L4	75 S E3
L5	144 S L1 OR L4
L6	62 S L2 OR L3
L7	204 S L5 OR L6
L8	10 S L7 AND HYPERTENSI?
L9	0 S L7 AND (CYCLIC GUANOSINE MONOPHOSPHATE (W) (PHOSPHODIESTERASE
L10	6 S L7 AND ("CGMP" OR "PDE5" OR "ANGIOTENSIN II RECEPTOR ANTAGONI

FILE 'REGISTRY' ENTERED AT 11:57:43 ON 02 MAR 2005

	E SILDENAFIL/CN
L11	2 S E3-E4
	E TADALAFIL/CN
L12	1 S E3
	E VARDENAFIL/CN
L13	3 S E3-E5
L14	1 S CANDESARTAN/CN
	E CANDESARTAN/CN
L15	2 S E3-E5
	E EPROSARTAN/CN
L16	2 S E3-E5
	E IRBESARTAN/CN
L17	4 S E3-E6
	E LOSARTAN/CN
L18	4 S E3-E7
	E OLMESARTAN/CN
L19	2 S E3-E5
	E SARALASIN/CN
L20	2 S E3-E4
	E TELMISARTAN/CN
L21	5 S E3-E7
	E VALSARTAN/CN
L22	2 S E3-E4
L23	6 S L11 OR L12 OR L13

L24

23 S L15 OR L16 OR L17 OR L18 OR L19 OR L20 OR L21 OR L22

FILE 'CAPLUS' ENTERED AT 12:02:01 ON 02 MAR 2005

L25 1081 S L23
 L26 4320 S L24
 E HYPERTENSION/BI
 L27 78751 S E3, E16
 E HYPERTENSION/CT
 L28 43383 S E3
 L29 78751 S L27 OR L28
 L30 80818 S L29 OR (HIGH BLOOD PRESSURE) OR (ELEVATED BLOOD PRESSURE) OR
 L31 36 S L25 AND L26
 L32 9 S L31 (L) L30
 L33 9 S L30 AND L31
 L34 34 S L25 (L) L30
 L35 1025 S L26 (L) L30
 L36 0 S L34 AND L35
 L37 9 S L31 AND HYPERTENS?
 L38 0 S L37 NOT L33
 L39 20335 S "CGMP" OR "PDE5" OR (CYCLIC GUANOSINE MONOPHOSPHATE (W) PHOSP
 L40 6539 S (ANGIOTENSIN (L) RECEPTOR ANTAGONIST) OR (ANGIOTENSIN RECEPTO
 L41 80 S L39 (L) L40
 L42 17 S L41 AND HYPERTENS?
 L43 16 S L42 NOT L33
 L44 115 S L31 OR L41
 L45 15 S L44 AND (ANGINA? OR STROKE? OR DIABET? OR CONGESTIVE HEART FA
 L46 11 S L45 NOT L43
 L47 6 S L46 NOT L33
 L48 5 S L46 NOT L47

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COST IN U.S. DOLLARS

 SINCE FILE
 ENTRY

 TOTAL
 SESSION

FULL ESTIMATED COST

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426.39

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

 SINCE FILE
 ENTRY

 TOTAL
 SESSION

CA SUBSCRIBER PRICE

-26.28

-37.96

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FILE 'WPIDS' ENTERED AT 12:19:37 ON 02 MAR 2005

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 => s (sildenafil? or viagra? or tadalafil? or "IC-351" or "IC 351" or "IC351" or
 cialis? or vardenafil? or levitra?_)

UNMATCHED LEFT PARENTHESIS '(SILDENAFIL'

 The number of right parentheses in a query must be equal to the
 number of left parentheses.

 => s (sildenafil? or viagra? or tadalafil? or "IC-351" or "IC 351" or "IC351" or
 cialis? or vardenafil? or levitra?_)

 L49 7998 (SILDENAFIL? OR VIAGRA? OR TADALAFIL? OR "IC-351" OR "IC 351"
 OR "IC351" OR CIALIS? OR VARDENAFIL? OR LEVITRA?_)

 => s (sildenafil? or viagra? or tadalafil? or "IC-351" or "IC 351" or "IC351" or
 cialis? or vardenafil? or levitra?)

L50 7998 (SILDENAFIL? OR VIAGRA? OR TADALAFIL? OR "IC-351" OR "IC 351"

OR "IC351" OR CIALIS? OR VARDENAFIL? OR LEVITRA?)

=> s (candesartan or "CV-11974" or "CV 11974" or "CV11974" or eprosartan? or teveten? or "SKF-108566" or "SKF 108566" or "SKF108566" or irbesartan? or "BMS-186295" or "BMS 186295" or "BMS186295" or "SR-47436" or "SR 47436" or "SR47436" or avapro? or aprovel? or karvea?)

L51 7887 (CANDESARTAN OR "CV-11974" OR "CV 11974" OR "CV11974" OR EPROSARTAN? OR TEVETEN? OR "SKF-108566" OR "SKF 108566" OR "SKF108566" OR IRBESARTAN? OR "BMS-186295" OR "BMS 186295" OR "BMS186295" OR "SR-47436" OR "SR 47436" OR "SR47436" OR AVAPRO? OR APROVEL? OR KARVEA?)

=> s losartan? or cozaar? or "DUP-753" or "DUP 753" or "DUP753" or "MK-954" or "MK954" or "MK 954" or olmesartan? or olmesartan medoxomil? or "CS-866" or "CS866" or "CS 866" or benicar? or olmetec? or votum?

L52 18908 LOSARTAN? OR COZAAR? OR "DUP-753" OR "DUP 753" OR "DUP753" OR "MK-954" OR "MK954" OR "MK 954" OR OLMESARTAN? OR OLMESARTAN MEDOXOMIL? OR "CS-866" OR "CS866" OR "CS 866" OR BENICAR? OR OLMETEC? OR VOTUM?

=> s saralasin? or "P-113" or "P 113" or "P113" or telmisartan? or "BIBR277" or "BIBR-277" or "BIBR 277" or pritor? or micardis? or valsartan? or diovan? or "CGP-48933" or "CGP 48933" or "CGP48933" or tareg? or kalpress? or miten? or nisis? or provas? or vals?

L53 26692 SARALASIN? OR "P-113" OR "P 113" OR "P113" OR TELMISARTAN? OR "BIBR277" OR "BIBR-277" OR "BIBR 277" OR PRITOR? OR MICARDIS? OR VALSARTAN? OR DIOVAN? OR "CGP-48933" OR "CGP 48933" OR "CGP48933" OR TAREG? OR KALPRESS? OR MITEN? OR NISIS? OR PROVAS? OR VALS?

=> d his

(FILE 'HOME' ENTERED AT 11:49:08 ON 02 MAR 2005)

FILE 'CAPLUS' ENTERED AT 11:49:13 ON 02 MAR 2005

L1 E FOX DAVID/AU
69 S E2-E3, E20-E22
E HUGHES BERNADETTE/AU
L2 22 S E3-E4
E HUGHES B/AU
L3 40 S E3
E FOX D/AU
E FOX D?/AU
E FOX D/AU
L4 75 S E3
L5 144 S L1 OR L4
L6 62 S L2 OR L3
L7 204 S L5 OR L6
L8 10 S L7 AND HYPERTENSI?
L9 0 S L7 AND (CYCLIC GUANOSINE MONOPHOSPHATE (W) (PHOSPHODIESTERASE
L10 6 S L7 AND ("CGMP" OR "PDE5" OR "ANGIOTENSIN II RECEPTOR ANTAGONI

FILE 'REGISTRY' ENTERED AT 11:57:43 ON 02 MAR 2005

L11 E SILDENAFIL/CN
2 S E3-E4
E TADALAFIL/CN
L12 1 S E3
E VARDENAFIL/CN
L13 3 S E3-E5
L14 1 S CANDESARTAN/CN
E CANDESARTAN/CN
L15 2 S E3-E5
E EPROSARTAN/CN
L16 2 S E3-E5

L17 4 E IRBESARTAN/CN
 4 S E3-E6
 L18 4 E LOSARTAN/CN
 4 S E3-E7
 E OLMESARTAN/CN
 L19 2 S E3-E5
 E SARALASIN/CN
 L20 2 S E3-E4
 E TELMISARTAN/CN
 L21 5 S E3-E7
 E VALSARTAN/CN
 L22 2 S E3-E4
 L23 6 S L11 OR L12 OR L13
 L24 23 S L15 OR L16 OR L17 OR L18 OR L19 OR L20 OR L21 OR L22

FILE 'CAPLUS' ENTERED AT 12:02:01 ON 02 MAR 2005

L25 1081 S L23
 L26 4320 S L24
 E HYPERTENSION/BI
 L27 78751 S E3, E16
 E HYPERTENSION/CT
 L28 43383 S E3
 L29 78751 S L27 OR L28
 L30 80818 S L29 OR (HIGH BLOOD PRESSURE) OR (ELEVATED BLOOD PRESSURE) OR
 L31 36 S L25 AND L26
 L32 9 S L31 (L) L30
 L33 9 S L30 AND L31
 L34 34 S L25 (L) L30
 L35 1025 S L26 (L) L30
 L36 0 S L34 AND L35
 L37 9 S L31 AND HYPERTENS?
 L38 0 S L37 NOT L33
 L39 20335 S "CGMP" OR "PDE5" OR (CYCLIC GUANOSINE MONOPHOSPHATE (W) PHOSP
 L40 6539 S (ANGIOTENSIN (L) RECEPTOR ANTAGONIST) OR (ANGIOTENSIN RECEPTO
 L41 80 S L39 (L) L40
 L42 17 S L41 AND HYPERTENS?
 L43 16 S L42 NOT L33
 L44 115 S L31 OR L41
 L45 15 S L44 AND (ANGINA? OR STROKE? OR DIABET? OR CONGESTIVE HEART FA
 L46 11 S L45 NOT L43
 L47 6 S L46 NOT L33
 L48 5 S L46 NOT L47

FILE 'MEDLINE, BIOSIS, EMBASE, WPIDS' ENTERED AT 12:19:37 ON 02 MAR 2005

L49 7998 S (SILDENAFIL? OR VIAGRA? OR TADALAFIL? OR "IC-351" OR "IC 351"
 L50 7998 S (SILDENAFIL? OR VIAGRA? OR TADALAFIL? OR "IC-351" OR "IC 351"
 L51 7887 S (CANDESARTAN OR "CV-11974" OR "CV 11974" OR "CV11974" OR EPRO
 L52 18908 S LOSARTAN? OR COZAAR? OR "DUP-753" OR "DUP 753" OR "DUP753" OR
 L53 26692 S SARALASIN? OR "P-113" OR "P 113" OR "P113" OR TELMISARTAN? OR

=> d cost

COST IN U.S. DOLLARS

	SINCE FILE ENTRY	TOTAL SESSION
CONNECT CHARGES	12.62	32.13
NETWORK CHARGES	0.48	3.54
SEARCH CHARGES	0.00	266.02
DISPLAY CHARGES	0.00	137.80
FULL ESTIMATED COST	13.10	439.49

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	0.00	-37.96

IN FILE 'MEDLINE, BIOSIS, EMBASE, WPIDS' AT 12:24:58 ON 02 MAR 2005

=> s 151 or 152 or 153

L54 48656 L51 OR L52 OR L53

=> s 150 and 154

L55 130 L50 AND L54

=> s 155 (L) (hypertens? or (high blood pressure? or elevated blood pressure? or (increase? blood pressure)))

PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH

FIELD CODE - 'AND' OPERATOR ASSUMED 'L79 (L) '

PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH

FIELD CODE - 'AND' OPERATOR ASSUMED 'L80 (L) '

PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH

FIELD CODE - 'AND' OPERATOR ASSUMED 'L81 (L) '

3 FILES SEARCHED...

PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH

FIELD CODE - 'AND' OPERATOR ASSUMED 'L82 (L) '

L56 46 L55 (L) (HYPERTENS? OR (HIGH BLOOD PRESSURE? OR ELEVATED BLOOD PRESSURE? OR (INCREASE? BLOOD PRESSURE)))

=> dup rem 156

PROCESSING COMPLETED FOR L56

L57 45 DUP REM L56 (1 DUPLICATE REMOVED)

ANSWER '1' FROM FILE MEDLINE

ANSWER '2' FROM FILE BIOSIS

ANSWERS '3-34' FROM FILE EMBASE

ANSWERS '35-45' FROM FILE WPIDS

=> d 157 1-45

THE ESTIMATED COST FOR THIS REQUEST IS 133.77 U.S. DOLLARS

DO YOU WANT TO CONTINUE WITH THIS REQUEST? (Y)/N:n

REQUEST CANCELED

=> s 155 and hypertens?

L58 46 L55 AND HYPERTENS?

=> d cost

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

CONNECT CHARGES

22.87

42.38

NETWORK CHARGES

0.78

3.84

SEARCH CHARGES

0.00

266.02

DISPLAY CHARGES

0.00

137.80

FULL ESTIMATED COST

23.65

450.04

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

SINCE FILE

TOTAL

ENTRY

SESSION

CA SUBSCRIBER PRICE

0.00

-37.96

IN FILE 'MEDLINE, BIOSIS, EMBASE, WPIDS' AT 12:27:36 ON 02 MAR 2005

=> d 157 scan

L57 45 ANSWERS WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN

AN 2003-720097 [68] WPIDS

TI Propellant free buccal spray composition used for increasing rapid absorption of active compounds, comprises active compound such as antiarrhythmic, antihypertensive, heart regulator or vasodilator and polar

solvent.

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):.

L57 45 ANSWERS WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN

AN 2001-475649 [51] WPIDS

TI Solid composition for delivery of active agents e.g. glyburide comprises carrier optionally containing a substrate having an encapsulation coat containing hydrophilic surfactants e.g. polyoxyethylene alkylethers.

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):.

L57 45 ANSWERS WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN

AN 2000-147185 [13] WPIDS

TI Nitrate salts of antihypertensive agents.

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):.

L57 45 ANSWERS BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN

TI Different effect of **valsartan** and lisinopril on **sildenafil** use in **hypertensive** men with erectile dysfunction.

IT Miscellaneous Descriptors
drug dosage; drug efficacy; Meeting Abstract

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):.

L57 45 ANSWERS WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN

AN 2004-525396 [50] WPIDS

TI New cyclopentyl substituted glutaramide derivatives are neutral endopeptidase inhibitors useful for the treatment or prevention of e.g. cardiovascular disease, **hypertension** and sexual dysfunction.

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):.

L57 45 ANSWERS WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN

AN 2004-525387 [50] WPIDS

TI New cyclopentyl substituted glutaramide derivatives useful as neutral endopeptidase selective inhibitors for treating or preventing conditions such as **hypertension**, female sexual dysfunction and male erectile dysfunction.

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):.

L57 45 ANSWERS WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN

AN 2004-091044 [09] WPIDS

TI Combination useful for treating **hypertension**, congestive heart failure and diabetes comprises a cyclic guanosine monophosphate specific phosphodiesterase type 5 inhibitor and an angiotensin II receptor antagonist.

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):.

L57 45 ANSWERS WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN

AN 2004-675638 [66] WPIDS

TI New 3-(1-(3-(1,3-benzothiazol-6-yl) propylcarbamoyl)cycloalkyl) propionic acid derivatives are neutral endopeptidase enzyme inhibitors useful for the treatment of e.g. stroke, glaucoma, obesity, metabolic disease and

epilepsy.

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):end

=> d his

(FILE 'HOME' ENTERED AT 11:49:08 ON 02 MAR 2005)

FILE 'CAPLUS' ENTERED AT 11:49:13 ON 02 MAR 2005

E FOX DAVID/AU
L1 69 S E2-E3, E20-E22
E HUGHES BERNADETTE/AU
L2 22 S E3-E4
E HUGHES B/AU
L3 40 S E3
E FOX D/AU
E FOX D?/AU
E FOX D/AU
L4 75 S E3
L5 144 S L1 OR L4
L6 62 S L2 OR L3
L7 204 S L5 OR L6
L8 10 S L7 AND HYPERTENSI?
L9 0 S L7 AND (CYCLIC GUANOSINE MONOPHOSPHATE (W) (PHOSPHODIESTERASE
L10 6 S L7 AND ("CGMP" OR "PDE5" OR "ANGIOTENSIN II RECEPTOR ANTAGONI

FILE 'REGISTRY' ENTERED AT 11:57:43 ON 02 MAR 2005

E SILDENAFIL/CN
L11 2 S E3-E4
E TADALAFIL/CN
L12 1 S E3
E VARDENAFIL/CN
L13 3 S E3-E5
L14 1 S CANDESARTAN/CN
E CANDESARTAN/CN
L15 2 S E3-E5
E EPROSARTAN/CN
L16 2 S E3-E5
E IRBESARTAN/CN
L17 4 S E3-E6
E LOSARTAN/CN
L18 4 S E3-E7
E OLMESARTAN/CN
L19 2 S E3-E5
E SARALASIN/CN
L20 2 S E3-E4
E TELMISARTAN/CN
L21 5 S E3-E7
E VALSARTAN/CN
L22 2 S E3-E4
L23 6 S L11 OR L12 OR L13
L24 23 S L15 OR L16 OR L17 OR L18 OR L19 OR L20 OR L21 OR L22

FILE 'CAPLUS' ENTERED AT 12:02:01 ON 02 MAR 2005

L25 1081 S L23
L26 4320 S L24
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L27 78751 S E3, E16
E HYPERTENSION/CT
L28 43383 S E3
L29 78751 S L27 OR L28
L30 80818 S L29 OR (HIGH BLOOD PRESSURE) OR (ELEVATED BLOOD PRESSURE) OR
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L32 9 S L31 (L) L30

L33 9 S L30 AND L31
 L34 34 S L25 (L) L30
 L35 1025 S L26 (L) L30
 L36 0 S L34 AND L35
 L37 9 S L31 AND HYPERTENS?
 L38 0 S L37 NOT L33
 L39 20335 S "CGMP" OR "PDE5" OR (CYCLIC GUANOSINE MONOPHOSPHATE (W) PHOSP
 L40 6539 S (ANGIOTENSIN (L) RECEPTOR ANTAGONIST) OR (ANGIOTENSIN RECEPTO
 L41 80 S L39 (L) L40
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 L46 11 S L45 NOT L43
 L47 6 S L46 NOT L33
 L48 5 S L46 NOT L47

FILE 'MEDLINE, BIOSIS, EMBASE, WPIDS' ENTERED AT 12:19:37 ON 02 MAR 2005

L49 7998 S (SILDENAFIL? OR VIAGRA? OR TADALAFIL? OR "IC-351" OR "IC 351"
 L50 7998 S (SILDENAFIL? OR VIAGRA? OR TADALAFIL? OR "IC-351" OR "IC 351"
 L51 7887 S (CANDESARTAN OR "CV-11974" OR "CV 11974" OR "CV11974" OR EPRO
 L52 18908 S LOSARTAN? OR COZAAR? OR "DUP-753" OR "DUP 753" OR "DUP753" OR
 L53 26692 S SARALASIN? OR "P-113" OR "P 113" OR "P113" OR TELMISARTAN? OR
 L54 48656 S L51 OR L52 OR L53
 L55 130 S L50 AND L54
 L56 46 S L55 (L) (HYPERTENS? OR (HIGH BLOOD PRESSURE? OR ELEVATED BLOO
 L57 45 DUP REM L56 (1 DUPLICATE REMOVED)
 L58 46 S L55 AND HYPERTENS?

=> s (l55 and hypertens?)/ab

QUALIFICATION NOT VALID FOR L55

Field code qualifications can only be applied to text terms.

=> d l57 1-45 trial

NO VALID FORMATS ENTERED FOR FILE 'BIOSIS'

In a multifile environment, each file must have at least one valid format requested. Refer to file specific help messages or the STNGUIDE file for information on formats available in individual files.

REENTER DISPLAY FORMAT FOR ALL FILES (FILEDEFAULT):title

'TITLE' IS NOT A VALID FORMAT

In a multifile environment, a format can only be used if it is valid in at least one of the files. Refer to file specific help messages or the STNGUIDE file for information on formats available in individual files.

REENTER DISPLAY FORMAT FOR ALL FILES (FILEDEFAULT):ti

L57 ANSWER 1 OF 45 MEDLINE on STN DUPLICATE 1
 TI Interactions between grapefruit juice and cardiovascular drugs.

L57 ANSWER 2 OF 45 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
 TI Different effect of **valsartan** and lisinopril on **sildenafil** use in **hypertensive** men with erectile dysfunction.

L57 ANSWER 3 OF 45 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
 on STN

TI New drugs approved by the FDA; New dosage forms and indications; Agents pending FDA approval; Significant labeling changes related to safety.

L57 ANSWER 4 OF 45 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
 on STN

TI Highlights of the year in JACC 2004.

L57 ANSWER 5 OF 45 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN
TI Drug-induced atrial fibrillation.

L57 ANSWER 6 OF 45 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN
TI Gateways to clinical trials: December 2004.

L57 ANSWER 7 OF 45 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN
TI Pilot assessment of the response of several pulmonary hemodynamic variables to sublingual **sildenafil** in candidates for heart transplantation.

L57 ANSWER 8 OF 45 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN
TI ACC/AHA guidelines for the management of patients with ST-elevation myocardial infarction - Executive summary: A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (writing committee to revise the 1999 guidelines for the management of patients with acute myocardial infarction).

L57 ANSWER 9 OF 45 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN
TI Gateways to Clinical Trials: July/August 2004.

L57 ANSWER 10 OF 45 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN
TI Stand by your brand.

L57 ANSWER 11 OF 45 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN
TI [New advances in drug therapy in 2003-2004].
ACTUALITES THERAPEUTIQUES 2003-2004 (1).

L57 ANSWER 12 OF 45 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN
TI Scleroderma - Clinical and pathological advances.

L57 ANSWER 13 OF 45 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN
TI Erectile dysfunction: A need for greater awareness.

L57 ANSWER 14 OF 45 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN
TI Diastolic dysfunction.

L57 ANSWER 15 OF 45 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN
TI The Year's New Drugs.

L57 ANSWER 16 OF 45 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN
TI The top 12 advances in vascular medicine.

L57 ANSWER 17 OF 45 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN
TI Pharmacy prepares for the leap year.

L57 ANSWER 18 OF 45 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN
TI Interactions of grapefruit juice and cardiovascular medications: A potential risk of toxicity.

L57 ANSWER 19 OF 45 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN
TI Active drug metabolites in drug development.

L57 ANSWER 20 OF 45 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN
TI New drug approvals for 2002.

L57 ANSWER 21 OF 45 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN
TI Sexual dysfunction in men and women with chronic kidney disease and end-stage kidney disease.

L57 ANSWER 22 OF 45 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN
TI New drugs with novel therapeutic characteristics. Have they been subject to randomized controlled trials?.

L57 ANSWER 23 OF 45 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN
TI Management of systemic sclerosis.

L57 ANSWER 24 OF 45 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN
TI [New advances in drug therapy in the year 2002].
ACTUALITES THERAPEUTIQUES 2002.

L57 ANSWER 25 OF 45 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN
TI Pulmonary **hypertension**: Current criteria for diagnosis and treatment.

L57 ANSWER 26 OF 45 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN
TI Erectile dysfunction and **hypertension**.

L57 ANSWER 27 OF 45 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN
TI Opinion and evidence in cardiovascular therapeutics.

L57 ANSWER 28 OF 45 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN
TI The choice of antihypertensive drugs in patients with erectile dysfunction.

L57 ANSWER 29 OF 45 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN
TI The effect of a **losartan**-based treatment regimen on isolated systolic **hypertension**.

L57 ANSWER 30 OF 45 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN
TI BMS takes Vanlev to the FDA.

L57 ANSWER 31 OF 45 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN
TI Lercanidipine: A novel dihydropyridine calcium-channel blocker.

L57 ANSWER 32 OF 45 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN
TI [Treatment of erectile dysfunction with **sildenafil** in patients with miocardic revascularization].
TRATAMENTO DA DISFUNCAO ERETIL COM **SILDENAFIL** EM PACIENTES COM

REVASCULARIZACAO MIOCARDICA.

-
- L57 ANSWER 33 OF 45 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN
TI **Sildenafil (viagra)**: Use and precautions in patients with cardiovascular disease.
- L57 ANSWER 34 OF 45 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN
TI New molecular entities approved in 1998.
- L57 ANSWER 35 OF 45 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
TI New cyclopentyl substituted glutaramide derivatives are neutral endopeptidase inhibitors useful for the treatment or prevention of e.g. cardiovascular disease, **hypertension** and sexual dysfunction.
- L57 ANSWER 36 OF 45 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
TI New cyclopentyl substituted glutaramide derivatives useful as neutral endopeptidase selective inhibitors for treating or preventing conditions such as **hypertension**, female sexual dysfunction and male erectile dysfunction.
- L57 ANSWER 37 OF 45 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
TI Combination useful for treating **hypertension**, congestive heart failure and diabetes comprises a cyclic guanosine monophosphate specific phosphodiesterase type 5 inhibitor and an angiotensin II receptor antagonist.
- L57 ANSWER 38 OF 45 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
TI New 3-(1-(3-(1,3-benzothiazol-6-yl) propylcarbamoyl)cycloalkyl) propionic acid derivatives are neutral endopeptidase enzyme inhibitors useful for the treatment of e.g. stroke, glaucoma, obesity, metabolic disease and epilepsy.
- L57 ANSWER 39 OF 45 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
TI Nifedipine composition used for treating angina pectoris and **hypertension**, includes particles of nifedipine or its salt, and surface stabilizer.
- L57 ANSWER 40 OF 45 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
TI Treatment of vascular condition e.g. sexual dysfunction, atherosclerosis involves administering a combination of at least two agents selected from anti-pressor agent, endothelin antagonist and sex hormone.
- L57 ANSWER 41 OF 45 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
TI New polycyclic guanine derivatives useful for treating urological, vascular and pulmonary disorders.
- L57 ANSWER 42 OF 45 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
TI Production of cationic non-viral delivery vehicle useful e.g. for DNA lipofection or targeted drug delivery, by conjugating steroid or other drug with polyamine and mixing with lipid.
- L57 ANSWER 43 OF 45 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
TI Propellant free buccal spray composition used for increasing rapid absorption of active compounds, comprises active compound such as antiarrhythmic, antihypertensive, heart regulator or vasodilator and polar solvent.
- L57 ANSWER 44 OF 45 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
TI Solid composition for delivery of active agents e.g. glyburide comprises carrier optionally containing a substrate having an encapsulation coat containing hydrophilic surfactants e.g. polyoxyethylene alkylethers.

L57 ANSWER 45 OF 45 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
TI Nitrate salts of antihypertensive agents.

=> d 157 2,4,16,22,25,26,28,29,37,39,40 ibib ed abs

L57 ANSWER 2 OF 45 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
ACCESSION NUMBER: 2002:355141 BIOSIS
DOCUMENT NUMBER: PREV200200355141
TITLE: Different effect of **valsartan** and lisinopril on
sildenafil use in **hypertensive** men with
erectile dysfunction.
AUTHOR(S): Fogari, Roberto [Reprint author]; Preti, Paola [Reprint
author]; Mugellini, Amedeo [Reprint author]; Derosa,
Giuseppe [Reprint author]; Marasi, Gianluigi [Reprint
author]; Corradi, Luca [Reprint author]; Zoppi, Annalisa
[Reprint author]; Poletti, Luigi [Reprint author]; Rinaldi,
Andrea [Reprint author]
CORPORATE SOURCE: Department of Internal Medicine and Therapeutics,
University of Pavia-IRCCS Policlinico S. Matteo, Pavia,
Italy
SOURCE: American Journal of Hypertension, (April, 2002) Vol. 15,
No. 4 Part 2, pp. 37A. print.
Meeting Info.: Seventeenth Annual Scientific Meeting of the
American Society of Hypertension. New York, N.Y., USA. May
14-18, 2002.
CODEN: AJHYE6. ISSN: 0895-7061.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 26 Jun 2002
Last Updated on STN: 26 Jun 2002
ED Entered STN: 26 Jun 2002
Last Updated on STN: 26 Jun 2002

L57 ANSWER 4 OF 45 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN
ACCESSION NUMBER: 2005015181 EMBASE
TITLE: Highlights of the year in JACC 2004.
AUTHOR: Demaria A.N.; Ben-Yehuda O.; Berman D.; Feld G.K.;
Greenberg B.H.; Knoke J.D.; Knowlton K.U.; Lew W.Y.W.;
Narula J.; Sahn D.; Tsimikas S.
CORPORATE SOURCE: . ademaria@usd.edu
SOURCE: Journal of the American College of Cardiology, (4 Jan 2005)
45/1 (137-153).
Refs: 108
ISSN: 0735-1097 CODEN: JACCDI
PUBLISHER IDENT.: S 0735-1097(04)02233-8
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 018 Cardiovascular Diseases and Cardiovascular Surgery
027 Biophysics, Bioengineering and Medical
Instrumentation
036 Health Policy, Economics and Management
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English

L57 ANSWER 16 OF 45 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN
ACCESSION NUMBER: 2005034923 EMBASE
TITLE: The top 12 advances in vascular medicine.
AUTHOR: Olin J.W.; Jang J.; Jaff M.R.; Beckman J.A.; Rooke T.
CORPORATE SOURCE: Dr. J.W. Olin, Department of Medicine, Mount Sinai School

of Medicine, Box 1033, One Gustave L. Levy Place, New York,
NY 10029, United States. jeffrey.olin@msnyuhealth.org

SOURCE: Journal of Endovascular Therapy, (2004) 11/SUPPL. 2
(II21-II31).
Refs: 82
ISSN: 1526-6028 CODEN: JENTFI
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 017 Public Health, Social Medicine and Epidemiology
018 Cardiovascular Diseases and Cardiovascular Surgery
036 Health Policy, Economics and Management
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English

AB In the past decade, impressive strides have been made in the diagnosis and management of atherosclerotic, aneurysmal, and thromboembolic diseases, thanks in large part to the explosive growth in both vascular biology and clinical vascular medicine. We review what we consider to be the top 12 advances in this field: the discovery of nitric oxide, the metabolic syndrome, new thrombophilic disorders, therapeutic angiogenesis, endoluminal treatment of chronic venous disease, and a variety of drugs, including **sildenafil**, cilostazol, low-molecular-weight heparins, oral direct thrombin inhibitors, clopidogrel, statins, and angiotensin-converting enzyme inhibitors and angiotensin-receptor blocking agents.

L57 ANSWER 22 OF 45 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
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ACCESSION NUMBER: 2002375393 EMBASE
TITLE: New drugs with novel therapeutic characteristics. Have they
been subject to randomized controlled trials?.
AUTHOR: Lexchin J.
CORPORATE SOURCE: Dr. J. Lexchin, 121 Walmer Rd., Toronto, Ont. M5R 2X8,
Canada. joel.lexchin@utoronto.ca
SOURCE: Canadian Family Physician, (1 Sep 2002) 48/SEPT.
(1487-1492).
Refs: 8
ISSN: 0008-350X CODEN: CFPHAJ
COUNTRY: Canada
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 017 Public Health, Social Medicine and Epidemiology
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English; French

AB Objective. To determine how many randomized controlled trials on the safety or efficacy of new drugs are published when these drugs are first marketed in Canada, and to determine the quality of the information in those trials. Design. A MEDLINE search was conducted on each drug identified as having novel therapeutic characteristics and first marketed between 1990 and 2000. Main Outcome Measures. Number of trials dealing with the safety or efficacy of each drug published at the time the drug was marketed. Number of patients taking the study drug, length of the trial, and type of control. Results. The number of trials varied substantially. For some drugs, there were more than 20 studies; for others only a single study. Many trials were small and short-term, and used placebo controls. Conclusion. Too few trials or inadequate trials on the safety and efficacy of new drugs are published when these drugs are first marketed in Canada. The lack of published trials means that physicians do not know whether results are generalizable to their patients, how to position the drug in relation to other treatments, or whether the drugs have long-term safety and efficacy.

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ACCESSION NUMBER: 2002192173 EMBASE
TITLE: Pulmonary **hypertension**: Current criteria for
diagnosis and treatment.
AUTHOR: Barbera J.A.
CORPORATE SOURCE: Dr. J.A. Barbera, Servei de Pneumologia, Hospital Clinic,
Universitat de Barcelona, Villarroel 170, 08036 Barcelona,
Spain. jbarbera@clinic.ub.es
SOURCE: Medicina Clinica, (27 Apr 2002) 118/15 (590-596).
Refs: 41
ISSN: 0025-7753 CODEN: MCLBA2
COUNTRY: Spain
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 006 Internal Medicine
015 Chest Diseases, Thoracic Surgery and Tuberculosis
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English

L57 ANSWER 26 OF 45 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN

ACCESSION NUMBER: 2002334549 EMBASE
TITLE: Erectile dysfunction and **hypertension**.
AUTHOR: Jackson G.
SOURCE: International Journal of Clinical Practice, (2002) 56/7
(491-493).
Refs: 15
ISSN: 1368-5031 CODEN: IJCPF
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Editorial
FILE SEGMENT: 006 Internal Medicine
018 Cardiovascular Diseases and Cardiovascular Surgery
028 Urology and Nephrology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English

L57 ANSWER 28 OF 45 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN

ACCESSION NUMBER: 2002165920 EMBASE
TITLE: The choice of antihypertensive drugs in patients with
erectile dysfunction.
AUTHOR: Khan M.A.; Morgan R.J.; Mikhailidis D.P.
CORPORATE SOURCE: Dr. D.P. Mikhailidis, Department of Clinical Biochemistry,
Roy. Free/Univ. Coll. Med. School, Royal Free Campus, Pond
Street, London NW3 2QG, United Kingdom.
mikhailidis@hotmail.com
SOURCE: Current Medical Research and Opinion, (2002) 18/2
(103-107).
Refs: 35
ISSN: 0300-7995 CODEN: CMROCX
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; (Short Survey)
FILE SEGMENT: 018 Cardiovascular Diseases and Cardiovascular Surgery
028 Urology and Nephrology
036 Health Policy, Economics and Management
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English

AB It is well established that **hypertension** and the more
traditional anti-**hypertensive** drugs are associated with erectile
dysfunction (ED). There is evidence showing that two antihypertensive

drugs - doxazosin and **losartan** - have a positive effect on erectile function. Therefore these drugs may decrease the incidence of ED in patients who need treatment for **hypertension**. Doxazosin and/or **losartan** can also be beneficial in patients who develop ED after starting treatment with other antihypertensive drugs. These options could, in turn, ensure better compliance and blood pressure control. A fall in the overall cost of treatment will also be anticipated if there is a reduced need for drugs prescribed for ED in patients with **hypertension**.

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ACCESSION NUMBER: 2002139468 EMBASE
TITLE: The effect of a **losartan**-based treatment regimen on isolated systolic **hypertension**.
AUTHOR: Cushman W.C.; Brady W.E.; Gazdick L.P.; Zeldin R.K.
CORPORATE SOURCE: Dr. W.C. Cushman, Veterans Affairs Medical Center, Preventive Medicine Section 111Q, 1030 Jefferson Avenue, Memphis, TN 38104, United States
SOURCE: Journal of Clinical Hypertension, (2002) 4/2 (101-107).
Refs: 23
ISSN: 1524-6175 CODEN: JCHYFN
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 006 Internal Medicine
018 Cardiovascular Diseases and Cardiovascular Surgery
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English

AB This study was conducted to compare the antihypertensive efficacy and tolerability, over 12 weeks, of a **losartan**-based treatment regimen and placebo in patients with isolated systolic **hypertension**. Three hundred eight patients ≥ 35 years of age with isolated systolic **hypertension**, defined as trough sitting blood pressure between 140 and 200 mm Hg systolic and between 70 and 89 mm Hg diastolic, were randomized to **losartan** 50 mg (n=157) or placebo (n=151) once daily, with titration as necessary to achieve a goal trough sitting systolic blood pressure (SBP) < 140 mm Hg. At baseline, mean trough sitting SBP was 140-159 mm Hg in 20.5% of patients, 160-179 mm Hg in 62.7%, and 180-200 mm Hg in 16.9%, and was similar in the two groups (**losartan**, 165.3 mm Hg; placebo, 166.1 mm Hg). At 12 weeks, mean trough sitting SBP decreased significantly ($p < 0.001$) in both the **losartan**-based treatment group (by 19.2 mm Hg) and in the placebo group (by 7.6 mm Hg). The reduction in sitting SBP was significantly greater for **losartan** than placebo (-11.6 mm Hg; 95% confidence interval, -14.8 to -8.4). In patients with isolated systolic **hypertension**, a once-daily **losartan**-based treatment regimen significantly lowered SBP. The **losartan**-based regimen exhibited antihypertensive efficacy that was superior to that of placebo, with a similar tolerability profile.

L57 ANSWER 37 OF 45 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
ACCESSION NUMBER: 2004-091044 [09] WPIDS
DOC. NO. CPI: C2004-037098
TITLE: Combination useful for treating **hypertension**, congestive heart failure and diabetes comprises a cyclic guanosine monophosphate specific phosphodiesterase type 5 inhibitor and an angiotensin II receptor antagonist.
DERWENT CLASS: B02
INVENTOR(S): FOX, D N A; HUGHES, B
PATENT ASSIGNEE(S): (FOX-D-I) FOX D N A; (HUGH-I) HUGHES B; (PFIZ) PFIZER INC; (PFIZ) PFIZER LTD

COUNTRY COUNT: 103
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2004002461	A2	20040108	(200409)*	EN	25
RW:	AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NL OA PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW				
W:	AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NI NO NZ OM PH PL PT RO RU SC SD SE SG SK SL TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW				
US 2004132731	A1	20040708	(200445)		
AU 2003242895	A1	20040119	(200447)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2004002461	A2	WO 2003-IB2657	20030616
US 2004132731	A1 Provisional	US 2002-396780P	20020717
		US 2003-603369	20030625
AU 2003242895	A1	AU 2003-242895	20030616

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2003242895	A1 Based on	WO 2004002461

PRIORITY APPLN. INFO: GB 2002-14784 20020626

ED 20040205

AN 2004-091044 [09] WPIDS

AB WO2004002461 A UPAB: 20040205

NOVELTY - Combination (I) of an inhibitor of cyclic guanosine monophosphate specific phosphodiesterase type 5 (PDE5) (A) and an angiotensin II receptor antagonist (B) for the preparation of a medicament for the palliative, curative or prophylactic treatment of **hypertension**, congestive heart failure, angina, stroke, diabetes and impaired glucose tolerance, is new.

DETAILED DESCRIPTION - Combination (I) of an inhibitor of cyclic guanosine monophosphate specific phosphodiesterase type 5 (PDE5) (A) and an angiotensin II receptor antagonist (B) for the preparation of a medicament for the palliative, curative or prophylactic treatment of **hypertension**, including essential **hypertension**, pulmonary **hypertension**, secondary **hypertension**, isolated systolic **hypertension**, **hypertension** associated with diabetes, **hypertension** associated with atherosclerosis and renovascular **hypertension**, congestive heart failure, angina, stroke, diabetes and impaired glucose tolerance, is new.

INDEPENDENT CLAIMS are also included for the following:

(1) A composition comprising (A) and (B); and

(2) A kit for treating **hypertension** comprising a first composition comprising (A) and a second composition comprising (B) and a container for the compositions.

ACTIVITY - Hypotensive; Respiratory-Gen.; Antidiabetic; Cardiovascular-Gen.; Antianginal; Cerebroprotective; Vasotropic.

MECHANISM OF ACTION - Cyclic guanosine monophosphate specific phosphodiesterase type 5 (PDE5) inhibitor; Angiotensin II receptor antagonist.

USE - (I) is useful for the palliative, curative or prophylactic treatment of **hypertension** (including essential **hypertension**, pulmonary **hypertension**, secondary

hypertension, isolated systolic hypertension, hypertension associated with diabetes, hypertension associated with atherosclerosis and renovascular hypertension), congestive heart failure, angina, stroke, diabetes and impaired glucose tolerance (claimed).

(I) was tested for its efficacy in rats. The results showed that (I) was effective for the fall of mean arterial pressure (MAP) to 32.6 mmHg which was significantly larger than the sum of the two individual effects (7.4 mmHg for PDE5 inhibitor and 3.2 mmHg for **candesartan**) (p=0.058).

ADVANTAGE - (I) is more potent and less toxic.
Dwg.0/0

L57 ANSWER 39 OF 45 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
ACCESSION NUMBER: 2004-478988 [45] WPIDS
CROSS REFERENCE: 2000-303363 [26]; 2001-281805 [29]; 2002-425895 [45];
2003-183864 [18]; 2003-708770 [67]; 2003-767190 [72];
2003-897031 [82]; 2004-190670 [18]; 2004-191100 [18];
2004-327673 [30]; 2004-579872 [56]; 2004-603323 [58];
2005-121249 [13]
DOC. NO. NON-CPI: N2004-377675
DOC. NO. CPI: C2004-178302
TITLE: Nifedipine composition used for treating angina pectoris
and **hypertension**, includes particles of
nifedipine or its salt, and surface stabilizer.
DERWENT CLASS: A96 B03 P34
INVENTOR(S): MERISKO-LIVERSIDGE, E
PATENT ASSIGNEE(S): (ELAN-N) ELAN PHARMA INT LTD
COUNTRY COUNT: 1
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
US 2004115134	A1	20040617	(200445)*		28

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE	
US 2004115134	A1	CIP of	US 1999-337675	19990622
		Cont of	US 2000-666539	20000921
		Cont of	US 2000-715117	20001120
		CIP of	WO 2001-US15983	20010518
		CIP of	US 2002-75443	20020215
		CIP of	US 2003-276400	20030115
		CIP of	US 2003-345312	20030116
			US 2003-712259	20031114

FILING DETAILS:

PATENT NO	KIND	PATENT NO	
US 2004115134	A1	Cont of	US 6375986
		CIP of	US 6592903

PRIORITY APPLN. INFO: US 2003-712259 20031114; US
1999-337675 19990622; US
2000-666539 20000921; US
2000-715117 20001120; WO
2001-US15983 20010518; US
2002-75443 20020215; US
2003-276400 20030115; US
2003-345312 20030116

ED 20040716

AN 2004-478988 [45] WPIDS
CR 2000-303363 [26]; 2001-281805 [29]; 2002-425895 [45]; 2003-183864 [18];
2003-708770 [67]; 2003-767190 [72]; 2003-897031 [82]; 2004-190670 [18];
2004-191100 [18]; 2004-327673 [30]; 2004-579872 [56]; 2004-603323 [58];
2005-121249 [13]

AB US2004115134 A UPAB: 20050224

NOVELTY - A nifedipine composition comprises particles of nifedipine or its salt, where the nifedipine particles have an effective average particle size of less than 2000 nm; and a surface stabilizer.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for a method of making a nifedipine composition comprising contacting particles of nifedipine or its salt with a surface stabilizer(s), providing a composition having an average particle size of less than 200 nm.

ACTIVITY - Antianginal; Hypotensive; Vasotropic.

MECHANISM OF ACTION - Calcium channel blocker.

USE - The invention is used as a vasodilating agent and a hypotensive medicament for the remedy of angina pectoris and **hypertension**.

ADVANTAGE - The invention can be readily absorbed by a human, or other animal, decreases frequency of dosing, improves clinical efficacy, and potentially reduces side effects.

DESCRIPTION OF DRAWING(S) - The figure shows the mean in vivo plasma profiles of nifedipine after single dosed, fasted, administration in humans.

Dwg.1/2

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ACCESSION NUMBER: 2004-294421 [27] WPIDS

CROSS REFERENCE: 2000-237773 [20]

DOC. NO. CPI: C2004-112620

TITLE: Treatment of vascular condition e.g. sexual dysfunction, atherosclerosis involves administering a combination of at least two agents selected from anti-pressor agent, endothelin antagonist and sex hormone.

DERWENT CLASS: B05

INVENTOR(S): ADAMS, M A; HALE, T M; HEATON, J P W

PATENT ASSIGNEE(S): (CALL-N) CALLEGY PHARM INC; (TOOH) UNIV QUEENS KINGSTON

COUNTRY COUNT: 1

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
US 2004063719	A1	20040401	(200427)*		29

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
US 2004063719	A1	Provisional	US 1998-98178P
		Cont of	US 1999-382749
		Cont of	US 2001-902787
		Provisional	US 2002-377917P
		CIP of	US 2002-192281
			US 2003-429197

FILING DETAILS:

PATENT NO	KIND	PATENT NO
US 2004063719	A1	Cont of
		Cont of
		US 6284763
		US 6458797

PRIORITY APPLN. INFO: US 2003-429197 20030502; US
1998-98178P 19980826; US
1999-382749 19990825; US

2001-902787 20010712; US
2002-377917P 20020502; US
2002-192281 20020709

ED 20040426
AN 2004-294421 [27] WPIDS
CR 2000-237773 [20]
AB US2004063719 A UPAB: 20040426
NOVELTY - Treatment of vascular condition involves administration of a combination of at least two agents selected from an anti-pressor agent, an endothelin antagonist and a sex hormone.
ACTIVITY - Vasotropic; Uropathic; Gynecological; Antiinflammatory; Antidiabetic; Antiarteriosclerotic; Nephrotropic; Hypotensive; Ophthalmological; Neuroprotective; Cardiant.
MECHANISM OF ACTION - None given.
USE - For treatment of vascular conditions such as male sexual dysfunction (e.g. erectile dysfunction, priapism and premature ejaculation), female sexual dysfunction (e.g. vaginal lubrication, vaginal engorgement, pain during intercourse, dyspareunia, urogenital infection, post-menopause, diabetes, vascular disease, estrogen depletion condition, idiosyncratic vaginal dryness, vaginismus, vulvodynia, interstitial cystitis, nonspecific urethritis, sexual arousal disorder, hypoactive desire disorder and sexual orgasmic disorder), atherosclerosis, renal failure, **hypertension**, congestive heart failure, diabetic retinopathy and diabetic neuropathy (all claimed).
ADVANTAGE - The endothelin antagonist eliminates or reduces anti-pressor tolerance. The combination therapy enhances the efficacy of the anti-pressor agent and enables increase in the frequency and duration of anti-pressor administration for long-term treatment of vascular conditions.
Dwg.0/10

=> d cost	SINCE FILE	TOTAL
	ENTRY	SESSION
COST IN U.S. DOLLARS		
CONNECT CHARGES	46.99	66.50
NETWORK CHARGES	1.38	4.44
SEARCH CHARGES	0.00	266.02
DISPLAY CHARGES	32.75	170.55
	-----	-----
FULL ESTIMATED COST	81.12	507.51
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE	TOTAL
	ENTRY	SESSION
CA SUBSCRIBER PRICE	0.00	-37.96

IN FILE 'MEDLINE, BIOSIS, EMBASE, WPIDS' AT 12:33:55 ON 02 MAR 2005

=> save
ENTER L#, L# RANGE, ALL, OR (END):end

=> d his

(FILE 'HOME' ENTERED AT 11:49:08 ON 02 MAR 2005)

FILE 'CAPLUS' ENTERED AT 11:49:13 ON 02 MAR 2005

	E FOX DAVID/AU
L1	69 S E2-E3, E20-E22
	E HUGHES BERNADETTE/AU
L2	22 S E3-E4
	E HUGHES B/AU
L3	40 S E3
	E FOX D/AU

E FOX D?/AU

E FOX D/AU

L4	75	S E3
L5	144	S L1 OR L4
L6	62	S L2 OR L3
L7	204	S L5 OR L6
L8	10	S L7 AND HYPERTENSI?
L9	0	S L7 AND (CYCLIC GUANOSINE MONOPHOSPHATE (W) (PHOSPHODIESTERASE
L10	6	S L7 AND ("CGMP" OR "PDE5" OR "ANGIOTENSIN II RECEPTOR ANTAGONI

FILE 'REGISTRY' ENTERED AT 11:57:43 ON 02 MAR 2005

		E SILDENAFIL/CN
L11	2	S E3-E4
		E TADALAFIL/CN
L12	1	S E3
		E VARDENAFIL/CN
L13	3	S E3-E5
L14	1	S CANDESARTAN/CN
		E CANDESARTAN/CN
L15	2	S E3-E5
		E EPROSARTAN/CN
L16	2	S E3-E5
		E IRBESARTAN/CN
L17	4	S E3-E6
		E LOSARTAN/CN
L18	4	S E3-E7
		E OLMESARTAN/CN
L19	2	S E3-E5
		E SARALASIN/CN
L20	2	S E3-E4
		E TELMISARTAN/CN
L21	5	S E3-E7
		E VALSARTAN/CN
L22	2	S E3-E4
L23	6	S L11 OR L12 OR L13
L24	23	S L15 OR L16 OR L17 OR L18 OR L19 OR L20 OR L21 OR L22

FILE 'CAPLUS' ENTERED AT 12:02:01 ON 02 MAR 2005

L25	1081	S L23
L26	4320	S L24
		E HYPERTENSION/BI
L27	78751	S E3, E16
		E HYPERTENSION/CT
L28	43383	S E3
L29	78751	S L27 OR L28
L30	80818	S L29 OR (HIGH BLOOD PRESSURE) OR (ELEVATED BLOOD PRESSURE) OR
L31	36	S L25 AND L26
L32	9	S L31 (L) L30
L33	9	S L30 AND L31
L34	34	S L25 (L) L30
L35	1025	S L26 (L) L30
L36	0	S L34 AND L35
L37	9	S L31 AND HYPERTENS?
L38	0	S L37 NOT L33
L39	20335	S "CGMP" OR "PDE5" OR (CYCLIC GUANOSINE MONOPHOSPHATE (W) PHOSP
L40	6539	S (ANGIOTENSIN (L) RECEPTOR ANTAGONIST) OR (ANGIOTENSIN RECEPTO
L41	80	S L39 (L) L40
L42	17	S L41 AND HYPERTENS?
L43	16	S L42 NOT L33
L44	115	S L31 OR L41
L45	15	S L44 AND (ANGINA? OR STROKE? OR DIABET? OR CONGESTIVE HEART FA
L46	11	S L45 NOT L43
L47	6	S L46 NOT L33
L48	5	S L46 NOT L47

FILE 'MEDLINE, BIOSIS, EMBASE, WPIDS' ENTERED AT 12:19:37 ON 02 MAR 2005

L49 7998 S (SILDENAFIL? OR VIAGRA? OR TADALAFIL? OR "IC-351" OR "IC 351"
L50 7998 S (SILDENAFIL? OR VIAGRA? OR TADALAFIL? OR "IC-351" OR "IC 351"
L51 7887 S (CANDESARTAN OR "CV-11974" OR "CV 11974" OR "CV11974" OR EPRO
L52 18908 S LOSARTAN? OR COZAAR? OR "DUP-753" OR "DUP 753" OR "DUP753" OR
L53 26692 S SARALASIN? OR "P-113" OR "P 113" OR "P113" OR TELMISARTAN? OR
L54 48656 S L51 OR L52 OR L53
L55 130 S L50 AND L54
L56 46 S L55 (L) (HYPERTENS? OR (HIGH BLOOD PRESSURE? OR ELEVATED BLOO
L57 45 DUP REM L56 (1 DUPLICATE REMOVED)
L58 46 S L55 AND HYPERTENS?

=> s l55 and (angina? or stroke? or diabet? or congestive heart failure?)

L59 28 L55 AND (ANGINA? OR STROKE? OR DIABET? OR CONGESTIVE HEART FAILU
RE?)

=> dup rem l59.

PROCESSING COMPLETED FOR L59

L60 27 DUP REM L59 (1 DUPLICATE REMOVED)
ANSWER '1' FROM FILE MEDLINE
ANSWERS '2-16' FROM FILE EMBASE
ANSWERS '17-27' FROM FILE WPIDS

=> d l60 1-27 ti

L60 ANSWER 1 OF 27 MEDLINE on STN DUPLICATE 1
TI Interactions between grapefruit juice and cardiovascular drugs.

L60 ANSWER 2 OF 27 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN
TI New drugs approved by the FDA; New dosage forms and indications; Agents
pending FDA approval; Significant labeling changes related to safety.

L60 ANSWER 3 OF 27 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN
TI Highlights of the year in JACC 2004.

L60 ANSWER 4 OF 27 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN
TI ACC/AHA guidelines for the management of patients with ST-elevation
myocardial infarction - Executive summary: A report of the American
College of Cardiology/American Heart Association Task Force on Practice
Guidelines (writing committee to revise the 1999 guidelines for the
management of patients with acute myocardial infarction).

L60 ANSWER 5 OF 27 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN
TI Gateways to Clinical Trials: July/August 2004.

L60 ANSWER 6 OF 27 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN
TI [New advances in drug therapy in 2003-2004].
ACTUALITES THERAPEUTIQUES 2003-2004 (1).

L60 ANSWER 7 OF 27 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN
TI Erectile dysfunction: A need for greater awareness.

L60 ANSWER 8 OF 27 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN
TI Diastolic dysfunction.

L60 ANSWER 9 OF 27 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.

on STN
TI Active drug metabolites in drug development.

L60 ANSWER 10 OF 27 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN

TI [Activities of the CPMP].
AKTIVITATEN DES CPMP.

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TI [New advances in drug therapy in the year 2002].
ACTUALITES THERAPEUTIQUES 2002.

L60 ANSWER 12 OF 27 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
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TI Opinion and evidence in cardiovascular therapeutics.

L60 ANSWER 13 OF 27 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
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TI BMS takes Vanlev to the FDA.

L60 ANSWER 14 OF 27 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
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TI Lercanidipine: A novel dihydropyridine calcium-channel blocker.

L60 ANSWER 15 OF 27 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
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TI Highlights of the **Diabetes** UK Annual Professional Meeting: 4-6
April 2001, Glasgow.

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TI **Sildenafil (viagra)**: Use and precautions in
patients with cardiovascular disease.

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TI Composition useful for the treatment of e.g. **diabetes** comprises
specific glipizide particles or its salt and at least one surface
stabilizer.

L60 ANSWER 18 OF 27 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN

TI Combination useful for treating hypertension, **congestive
heart failure** and **diabetes** comprises a cyclic
guanosine monophosphate specific phosphodiesterase type 5 inhibitor and an
angiotensin II receptor antagonist.

L60 ANSWER 19 OF 27 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN

TI New 3-(1-(3-(1,3-benzothiazol-6-yl) propylcarbamoyl)cycloalkyl) propionic
acid derivatives are neutral endopeptidase enzyme inhibitors useful for
the treatment of e.g. **stroke**, glaucoma, obesity, metabolic
disease and epilepsy.

L60 ANSWER 20 OF 27 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN

TI Nifedipine composition used for treating **angina pectoris** and
hypertension, includes particles of nifedipine or its salt, and surface
stabilizer.

L60 ANSWER 21 OF 27 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN

TI Treatment of vascular condition e.g. sexual dysfunction, atherosclerosis
involves administering a combination of at least two agents selected from
anti-pressor agent, endothelin antagonist and sex hormone.

L60 ANSWER 22 OF 27 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN

TI New polycyclic guanine derivatives useful for treating urological,

vascular and pulmonary disorders.

L60 ANSWER 23 OF 27 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
TI Production of cationic non-viral delivery vehicle useful e.g. for DNA lipofection or targeted drug delivery, by conjugating steroid or other drug with polyamine and mixing with lipid.

L60 ANSWER 24 OF 27 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
TI Bioerodible, water-soluble, carrier device for loading or delivering drug or active agent, comprises non-bioadhesive backing layer, bioadhesive layer and composition comprising active ingredient.

L60 ANSWER 25 OF 27 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
TI Propellant free buccal spray composition used for increasing rapid absorption of active compounds, comprises active compound such as antiarrhythmic, antihypertensive, heart regulator or vasodilator and polar solvent.

L60 ANSWER 26 OF 27 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
TI Solid composition for delivery of active agents e.g. glyburide comprises carrier optionally containing a substrate having an encapsulation coat containing hydrophilic surfactants e.g. polyoxyethylene alkylethers.

L60 ANSWER 27 OF 27 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
TI Treating senescence induced hypoxia of liver using vasodilating agent.

=> save

ENTER L#, L# RANGE, ALL, OR (END):all

ENTER NAME OR (END):110603369/1

L# LIST L1-L60 HAS BEEN SAVED AS 'L10603369/L'

=> d cost

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
CONNECT CHARGES	66.39	85.90
NETWORK CHARGES	2.10	5.16
SEARCH CHARGES	0.00	266.02
DISPLAY CHARGES	32.75	170.55
	-----	-----
FULL ESTIMATED COST	101.24	527.63
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	0.00	-37.96

IN FILE 'MEDLINE, BIOSIS, EMBASE, WPIDS' AT 12:40:23 ON 02 MAR 2005

=> d his

(FILE 'HOME' ENTERED AT 11:49:08 ON 02 MAR 2005)

FILE 'CAPLUS' ENTERED AT 11:49:13 ON 02 MAR 2005

L1 E FOX DAVID/AU
69 S E2-E3, E20-E22
E HUGHES BERNADETTE/AU

L2 22 S E3-E4
E HUGHES B/AU

L3 40 S E3
E FOX D/AU
E FOX D?/AU
E FOX D/AU

L4 75 S E3

L5 144 S L1 OR L4
L6 62 S L2 OR L3
L7 204 S L5 OR L6
L8 10 S L7 AND HYPERTENSI?
L9 0 S L7 AND (CYCLIC GUANOSINE MONOPHOSPHATE (W) (PHOSPHODIESTERASE
L10 6 S L7 AND ("CGMP" OR "PDE5" OR "ANGIOTENSIN II RECEPTOR ANTAGONI

FILE 'REGISTRY' ENTERED AT 11:57:43 ON 02 MAR 2005

E SILDENAFIL/CN
L11 2 S E3-E4
E TADALAFIL/CN
L12 1 S E3
E VARDENAFIL/CN
L13 3 S E3-E5
L14 1 S CANDESARTAN/CN
E CANDESARTAN/CN
L15 2 S E3-E5
E EPROSARTAN/CN
L16 2 S E3-E5
E IRBESARTAN/CN
L17 4 S E3-E6
E LOSARTAN/CN
L18 4 S E3-E7
E OLMESARTAN/CN
L19 2 S E3-E5
E SARALASIN/CN
L20 2 S E3-E4
E TELMISARTAN/CN
L21 5 S E3-E7
E VALSARTAN/CN
L22 2 S E3-E4
L23 6 S L11 OR L12 OR L13
L24 23 S L15 OR L16 OR L17 OR L18 OR L19 OR L20 OR L21 OR L22

FILE 'CAPLUS' ENTERED AT 12:02:01 ON 02 MAR 2005

L25 1081 S L23
L26 4320 S L24
E HYPERTENSION/BI
L27 78751 S E3, E16
E HYPERTENSION/CT
L28 43383 S E3
L29 78751 S L27 OR L28
L30 80818 S L29 OR (HIGH BLOOD PRESSURE) OR (ELEVATED BLOOD PRESSURE) OR
L31 36 S L25 AND L26
L32 9 S L31 (L) L30
L33 9 S L30 AND L31
L34 34 S L25 (L) L30
L35 1025 S L26 (L) L30
L36 0 S L34 AND L35
L37 9 S L31 AND HYPERTENS?
L38 0 S L37 NOT L33
L39 20335 S "CGMP" OR "PDE5" OR (CYCLIC GUANOSINE MONOPHOSPHATE (W) PHOSP
L40 6539 S (ANGIOTENSIN (L) RECEPTOR ANTAGONIST) OR (ANGIOTENSIN RECEPTO
L41 80 S L39 (L) L40
L42 17 S L41 AND HYPERTENS?
L43 16 S L42 NOT L33
L44 115 S L31 OR L41
L45 15 S L44 AND (ANGINA? OR STROKE? OR DIABET? OR CONGESTIVE HEART FA
L46 11 S L45 NOT L43
L47 6 S L46 NOT L33
L48 5 S L46 NOT L47

FILE 'MEDLINE, BIOSIS, EMBASE, WPIDS' ENTERED AT 12:19:37 ON 02 MAR 2005

L49 7998 S (SILDENAFIL? OR VIAGRA? OR TADALAFIL? OR "IC-351" OR "IC 351"

L50 7998 S (SILDENAFIL? OR VIAGRA? OR TADALAFIL? OR "IC-351" OR "IC 351"
L51 7887 S (CANDESARTAN OR "CV-11974" OR "CV 11974" OR "CV11974" OR EPRO
L52 18908 S LOSARTAN? OR COZAAR? OR "DUP-753" OR "DUP 753" OR "DUP753" OR
L53 26692 S SARALASIN? OR "P-113" OR "P 113" OR "P113" OR TELMISARTAN? OR
L54 48656 S L51 OR L52 OR L53
L55 130 S L50 AND L54
L56 46 S L55 (L) (HYPERTENS? OR (HIGH BLOOD PRESSURE? OR ELEVATED BLOO
L57 45 DUP REM L56 (1 DUPLICATE REMOVED)
L58 46 S L55 AND HYPERTENS?
L59 28 S L55 AND (ANGINA? OR STROKE? OR DIABET? OR CONGESTIVE HEART FA
L60 27 DUP REM L59 (1 DUPLICATE REMOVED)
SAVE ALL L10603369/L